This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

10/ 068,114

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

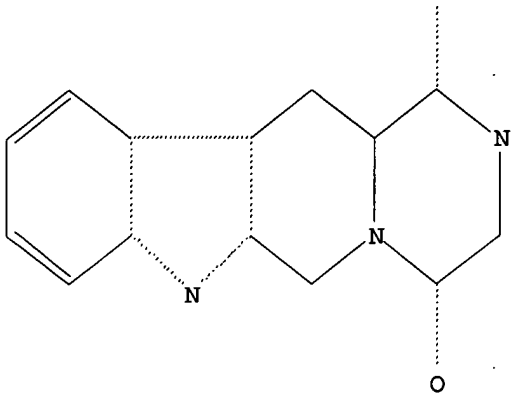
* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation
NEWS 38	AUG 18	Simultaneous left and right truncation added to ANABSTR

10/ 068,114

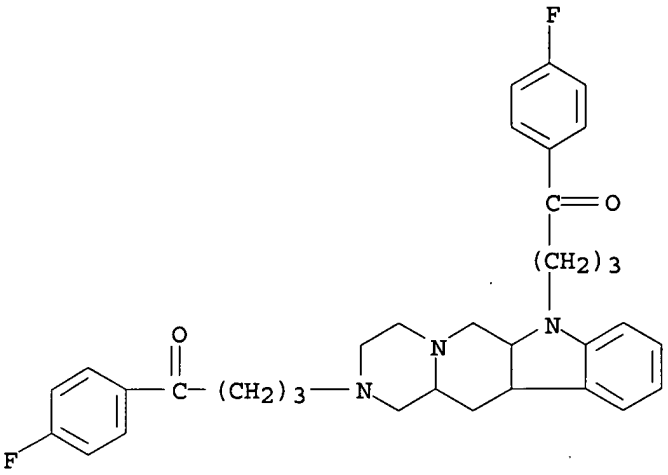
```
 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 07:36:56 ON 11 SEP 2003

=> file reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.21       0.21

FILE 'REGISTRY' ENTERED AT 07:37:02 ON 11 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    9 SEP 2003  HIGHEST RN 582289-61-0
DICTIONARY FILE UPDATES:   9 SEP 2003  HIGHEST RN 582289-61-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10068114.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
```

10/ 068,114



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 ful
FULL SEARCH INITIATED 07:37:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    292 TO ITERATE

100.0% PROCESSED     292 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01

L2             0 SEA SSS FUL L1

=> s octahydropyrazino
L3           21 OCTAHYDROPYRAZINO

=> d scan l3

L3    21 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS on STN
IN    1-Butanone, 4,4'-(1,3,4,6,6a,11b,12,12a-octahydropyrazino[1',2':1,6]p
      yrido[3,4-b]indole-2,7-diyl)bis[1-(4-fluorophenyl)-, monohydrochloride
      (9CI)
MF    C34 H37 F2 N3 O2 . Cl H
```



● HCl

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	153.57	153.78

FILE 'CAPLUS' ENTERED AT 07:39:29 ON 11 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 11 Sep 2003 VOL 139 ISS 11
FILE LAST UPDATED: 10 Sep 2003 (20030910/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 40 L3

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 40 ANSWERS - CONTINUE? Y/(N):y

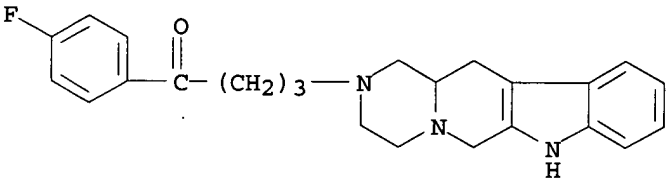
L4 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:251375 CAPLUS

10/ 068,114

TITLE: QSAR studies in substituted 1,2,3,4,6,7,12,12a-octa-hydropyrazino[2',1':6,1]pyrido[3,4-b]indoles-a potent class of neuroleptics
AUTHOR(S): Saxena, Anil K.; Ram, Siya; Saxena, Mridula; Singh, Nidhi; Prathipati, Philip; Jain, Padam C.; Singh, H. K.; Anand, Nitya
CORPORATE SOURCE: Cattar Manzil Palace Medicinal Chemistry Division, Central Drug Research Institute, Lucknow, 226001, India
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(9), 2085-2090
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of nineteen substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3, 4-b]indoles analogs of neuroleptic drug, Centbutindole have been studied using quant. structure-activity relationship anal. The derived models display good fits to the exptl. data (r>or=0.75) having good predictive power (rcv>or=0.688). The best model describes a high correlation between predicted and exptl. activity data (r=0.967). Statistical anal. of the equation populations indicates that hydrophobicity (as measured by .pi.R, logP(o/w) and SlogP_VSA8), dipole y and structural parameters in terms of indicator variable, (In1) and globularity are important variables in describing the variation in the neuroleptic activity in the series.

IT INDEXING IN PROGRESS
IT **42021-34-1DP**, Centbutindole, analogs
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(QSAR studies in substituted 1,2,3,4,6,7,12,12a-octa-hydropyrazino[2',1':6,1]pyrido[3,4-b]indoles, a potent class of neuroleptics)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:477833 CAPLUS
DOCUMENT NUMBER: 137:288014
TITLE: Basicity and coordination ability of linear hexa-amines in relation to N-(CH2)n-N chain-link lengths. A solution study
AUTHOR(S): Bencini, Andrea; Berni, Emanuela; Chuburu, Francoise; Giorgi, Claudia; Handel, Henri; Le Baccon, Michel; Paoletti, Piero; Valtancoli, Barbara
CORPORATE SOURCE: Department of Chemistry, University of Florence, Florence, Sesto Fiorentino, 50019, Italy
SOURCE: Polyhedron (2002), 21(14-15), 1459-1467

10/ 068,114

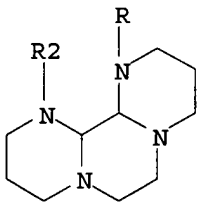
CODEN: PLYHDE; ISSN: 0277-5387
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

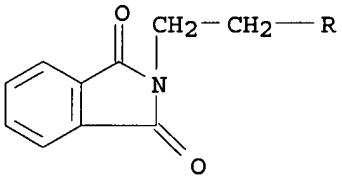
AB The synthesis of the two new linear hexa-amines, 3,7,10,14-tetraazahexadecane-1,16-diamine (L1) and 5,9,12,16-tetraazaicosane-1,20-diamine (L2) is reported. Ligand protonation and Cu(II) and Zn(II) coordination were studied in aq. soln. by potentiometric, microcalorimetric (298.1 K, I = 0.1 mol dm-3) and spectrophotometric (UV-visible, 1H and 13C NMR) measurements. The species present in soln. and their stability consts. were detd. L1 forms mono- and binuclear complexes in aq. soln. with Cu(II). In the [ML1]2+ complexes, the metal ion is coordinated by five N atoms, while in the [ML2]2+ complexes the metal ion is four-coordinate. This different behavior is explained in terms of the different nos. of methylene groups between adjacent N atoms.

IT **464927-98-8P 464927-99-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deprotection of)

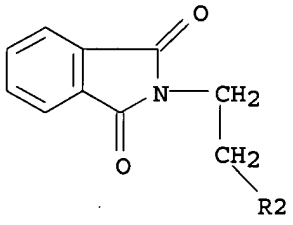
RN 464927-98-8 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2,2'-[(octahydropyrazino[1,2-a:4,3-a']dipyrimidine-1,12(2H,9H)-diyl)di-2,1-ethanediyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

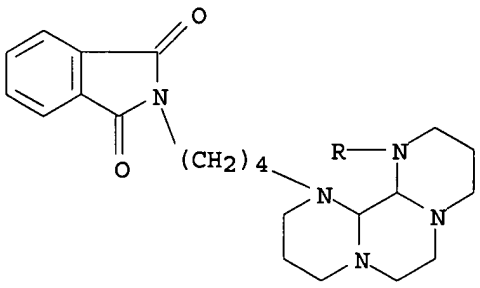


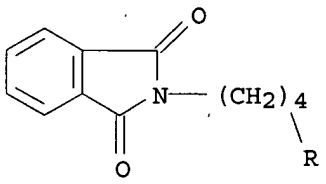


PAGE 2-A



RN 464927-99-9 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2,2'-[(octahydropyrazino[1,2-a:4,3-a']dipyrimidine-1,12(2H,9H)-diyl)di-4,1-butanediyl]bis- (9CI) (CA INDEX NAME)





REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

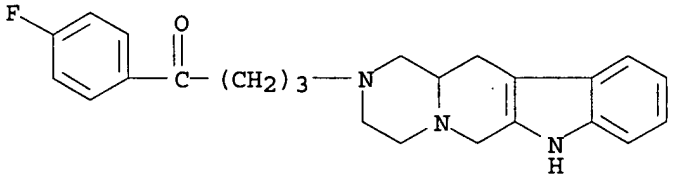
L4 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:771974 CAPLUS
DOCUMENT NUMBER: 136:177415
TITLE: A sensitive LC assay for the simultaneous determination of centbutindole and its metabolite in rat serum using fluorescence detection
AUTHOR(S): Issar, Manish; Singh, Shio Kumar; Mishra, Bhrameshwar; Gupta, Ram Chandra
CORPORATE SOURCE: Pharmacokinetics and Metabolism Division, Central Drug Research Institute, Lucknow, 226001, India
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2002), 27(1-2), 347-353
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Centbutindole (.+-.)-2-.gamma.-[(p-fluorobenzoyl)propyl]-1,2,3,4,6,7,12,12a-octahydropyrazino(2',1':6,1)yrido[3, 4-b] indole (I), is a new neuroleptic agent developed by Central Drug Research Institute, India. A HPLC assay method for the simultaneous assay for I and its metabolite (II) in rat serum was developed and validated. The present method requires only 1 mL of serum with detection levels similar to that reported earlier using 4 mL serum. This assay is more suited for pre-clin. as well as phase IV studies. Linearity was obsd. between 1.25 and 40 ng/mL for I and 0.625 and 20 ng/mL for II in rat serum. Recoveries were consistent for both the analytes over the concn. ranges studied. Variation in intra-and inter-batch accuracy and precision were within acceptable limits of .+-.20% at lowest limit of quantitation, whereas at higher concns. it was .+-.15%. The assay method was employed for the study of the pharmacokinetics and metab. of I in rats. The parent compd. and its metabolites were quantitated in serum and could be monitored up to 24 h post dose.

IT **42021-34-1**, Centbutindole
RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(a sensitive LC assay for the simultaneous detn. of centbutindole and its metabolite in rat serum using fluorescence detection)

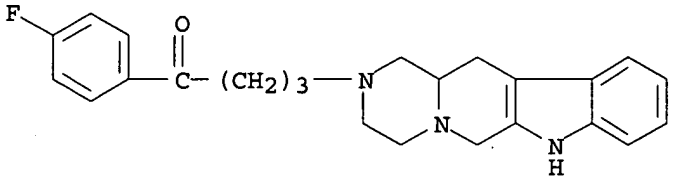
10/ 068,114

RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

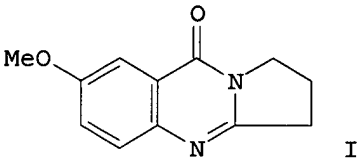


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

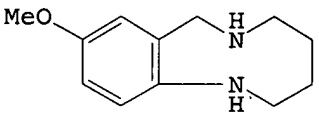
L4 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:1004133 CAPLUS
DOCUMENT NUMBER: 124:105604
TITLE: Comparison of molecular properties of D2-receptor antagonists from different chemical families of neuroleptics
AUTHOR(S): Rusig, Isabelle; Laguerre, Michel; Carpy, Alain; Saxena, Anil K.
CORPORATE SOURCE: Laboratoire Chemie Analytique, Universite Bordeaux II, Bordeaux, 33076, Fr.
SOURCE: Medicinal Chemistry Research (1995), 5(8), 631-45
CODEN: MCREEB; ISSN: 1054-2523
PUBLISHER: Birkhaeuser
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The literature about the geometrical binding requirements of selected dopamine antagonists is discussed. Up to now, the published results were mainly concerned with semirigid compds. which mostly belonged to one single family of neuroleptics. The authors, therefore, undertook a conformational study of nine D2-receptor antagonists belonging to different chem. families, including semirigid and flexible compds., and the hitherto not studied D2-receptor antagonist (-)-centbutindole to characterize the bioactive forms. Examn. of the best structural overlap of the common features of all mols. based on a postulated active form of (S)-octoclothepin helped in the identification of the other active conformers. At a second level of characterization, electronic and lipophilic properties of the active forms were computed to identify those properties responsible for the modulation of receptor recognition.
IT **42021-34-1**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(comparison of mol. properties of D2-receptor antagonists from different chem. families of neuroleptics)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:269233 CAPLUS
DOCUMENT NUMBER: 120:269233
TITLE: Sodium borohydride-boron trifluoride ethereate, a convenient and efficient reagent for the reduction of amides
AUTHOR(S): Sengupta, Sreela; Sahu, Devi P.; Chatterjee, Sunil K.
CORPORATE SOURCE: Div. Chem. Technol., Central Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1994), 33B(3), 285-7
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:269233
GI



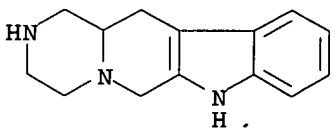
I



II

AB Sodium borohydride-boron trifluoride etherate has been employed as a reducing agent for the conversion of amides into amines, the reducing species being diborane generated in situ. This method successfully reduces primary, secondary and tertiary amides, lactams and chiral diketopiperazines, in moderate to high yields. An unusual ring cleavage is obsd. in the redn. of the pyrrolo[2,1-b]quinazolin-1-one (I) resulting in the formation of benzo-1,6-diazonine (II).

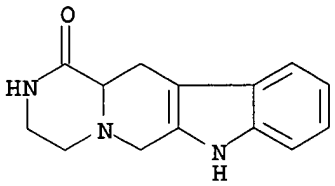
IT **55344-28-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



IT **55344-27-9**
RL: RCT (Reactant); RACT (Reactant or reagent)

10/ 068,114

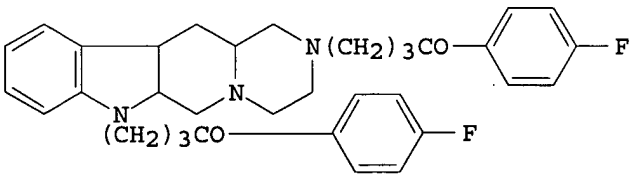
(redn. of, to amine with sodium borohydride-boron trifluoride ethereate)
RN 55344-27-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:124563 CAPLUS
DOCUMENT NUMBER: 118:124563
TITLE: A process for the synthesis of 2,7-bis-.gamma.-[(4-fluorobenzoyl)propyl]-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[2',1':6,1]pyrido(3,4-b)indole useful as potential CNS depressant agent
INVENTOR(S): Rao, Jyoti; Saxena, Anil Kumar; Dua, Prithvi Raj; Shankar, Girja; Bhalla, Vishwa Nath
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India
SOURCE: Indian, 6 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

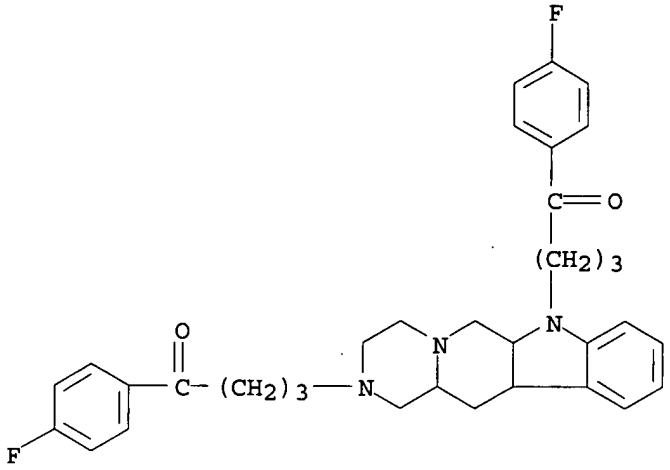
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 168877	A	19910629	IN 1987-DE1080	19871216

PRIORITY APPLN. INFO.: IN 1987-DE1080 19871216
GI

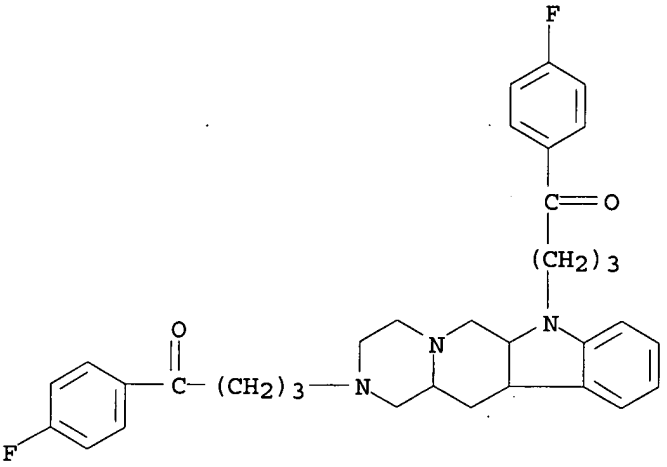


I

AB Title compd. (I), useful for treatment of psychic disorders (no data) was prepd. by condensation of 1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[2',1':6,1]pyrido(3,4-b)indole (II) with 4-FC6H4CO(CH2)3Cl (III) at 30-120.degree. in presence of base and org. solvent. III in DMF was added to II, NaCO3 and NaI in DMF, stirred at 70.degree. for 12 h to give I isolated as the HCl salt.
IT **146368-72-1P 146368-73-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as central nervous system depressant agent)
RN 146368-72-1 CAPLUS
CN 1-Butanone, 4,4'-(1,3,4,6,6a,11b,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-2,7-diyl)bis[1-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 146368-73-2 CAPLUS
CN 1-Butanone, 4,4'-(1,3,4,6,6a,11b,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-2,7-diyl)bis[1-(4-fluorophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

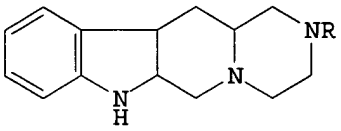
L4 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:591872 CAPLUS
DOCUMENT NUMBER: 117:191872
TITLE: Process for synthesis of novel 2-substituted-1,2,3,4,6,6a,7,11b,12,12a-decahydropyrazino[2,1:6,1]pyrido[3,4-b]indoles
INVENTOR(S): Rao, Jyoti; Saxena, Anil Kumar; Saxena, Ram Mohan; Dua, Prithviraj; Srimal, Rikhab Chand; Bhalla, Vishnunath
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India
SOURCE: Indian, 6 pp.

10/ 068,114

CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 166420	A	19900505	IN 1988-DE73	19880129

PRIORITY APPLN. INFO.: IN 1988-DE73 19880129
OTHER SOURCE(S): MARPAT 117:191872
GI

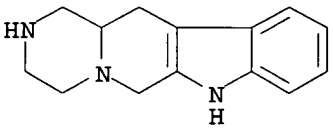


I

AB Title compds. I (R = H, alkyl) useful as starting materials for central nervous system and cardiovascular (sic) active agents, are prepd. by redn. of the octahydro deriv. at -20 to +5.degree. in 15 min to 24 h. Borane Me sulfide in soln. was added to the octahydro deriv. of I (R = H) in F3CCO2H at 0 to 50.degree. under N, then the reaction mixt. was stirred for 2 h at 34.degree. to give after basification I (R = H).

IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(redn. of, by borane Me sulfide)

RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:542817 CAPLUS
DOCUMENT NUMBER: 117:142817
TITLE: Single oral dose pharmacokinetics of centbutindole, a new neuroleptic agent, in healthy human volunteers
AUTHOR(S): Paliwal, J. K.; Gupta, R. C.; Grover, P. K.; Asthana, O. P.; Nityanand, S.
CORPORATE SOURCE: Pharmacokinet. Metab. Div., Cent. Drug Res. Inst., Lucknow, India
SOURCE: Drug Investigation (1992), 4(3), 246-51
CODEN: DRUIEA; ISSN: 0114-2402
DOCUMENT TYPE: Journal
LANGUAGE: English

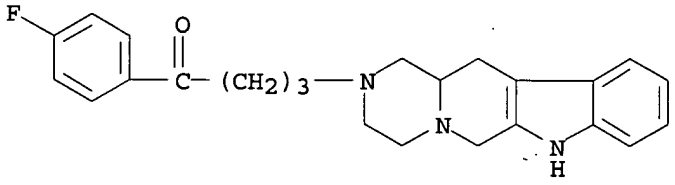
AB The pharmacokinetics of centbutindole compd. were investigated after oral administration of single 3 mg tables in 5 healthy male volunteers. Serum levels of the unchanged drug were measured by high pressure liq. chromatog. (HPLC) with fluorescence detection. Mean peak serum levels (3.48 .+-. 1.58 mg/L) were reached at 4 h, and the mean biol. half-life was calcd. as 12.45 .+-. 3.59 h. The data were best fitted to a

1-compartment open model with first-order absorption and elimination kinetics. Considerable intersubject variability was noted in the absorption characteristics of centbutindole, and further study is planned to better define the pharmacokinetics of this drug.

IT **42021-34-1**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacokinetics of, in humans)

RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1992:462715 CAPLUS

DOCUMENT NUMBER: 117:62715

TITLE: Antihistaminic activity of quinethindole: a 2-substituted pyrazinopyridoindole derivative

AUTHOR(S): Patnaik, G. K.; Saxena, A. K.; Saxena, M.; Srimal, R. C.

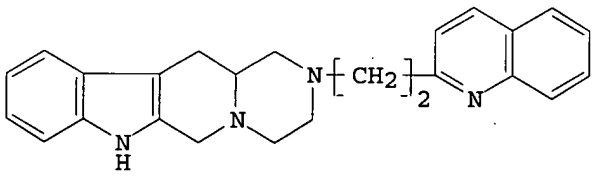
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Experimental Biology (1992), 30(2), 144-6
CODEN: IJEBA6; ISSN: 0019-5189

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

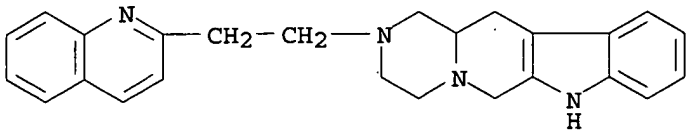
AB Quinethindole (I), a 2-substituted pyrazinopyridoindole, showed specific antihistaminic H1 activity in various in vivo and in vitro test models. It also inhibited antigen-induced contraction of ileum of sensitized guinea pig. The antihistaminic activity was of competitive nature.

IT **42021-23-8**, Quinethindole
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antihistaminic H1 activity of)

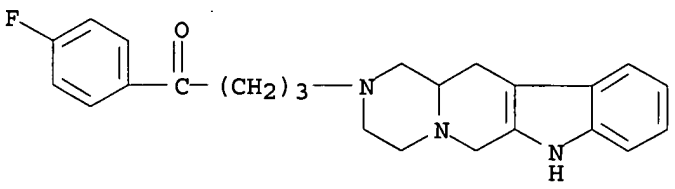
RN 42021-23-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(2-quinolinyl)ethyl]- (9CI) (CA INDEX NAME)

10/ 068,114



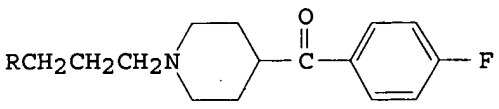
L4 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:50746 CAPLUS
DOCUMENT NUMBER: 116:50746
TITLE: Simultaneous determination of centbutindole and its hydroxy metabolite in serum by high-performance liquid chromatography
AUTHOR(S): Paliwal, Jyoti Kumar; Gupta, Ram Chandra; Grover, Pyara Krishen; Asthana, Omkar P.; Nityanand, Swaran
CORPORATE SOURCE: Pharmacokinet. Metab. Div., Cent. Drug. Res. Inst., Lucknow, 226001, India
SOURCE: Journal of Chromatography (1991), 572(1-2), 219-25
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A high-performance liq. chromatog. assay has been developed and validated for the detn. of centbutindole and its hydroxy metabolite in serum. The method involves extn. of serum samples with di-Et ether at pH > 8, back-extn. into 0.5 M hydrochloric acid and finally again with di-Et ether after addn. of 2 M potassium hydroxide. Sepn. was accomplished by reversed-phase high-performance liq. chromatog. on a cyano column with an acetonitrile-phosphate buffer system. The recovery of centbutindole and its metabolite was always greater than 80%. Calibration curves were linear over the concn. range 0.25-5 ng/mL for centbutindole and 0.05-1 ng/mL for the hydroxy metabolite. Although the lower limit of detection was 0.1 ng/mL for centbuntindole and 0.02 ng/mL for the hydroxy metabolite, the reliable limits of quantitation were 0.25 and 0.05 ng/mL, resp., using 4 mL of serum.
IT **42021-34-1**, Centbutindole
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in blood of humans by HPLC)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:6251 CAPLUS
DOCUMENT NUMBER: 114:6251
TITLE: Synthesis and SAR studies in 1-(.gamma.-substituted propyl)-4-(4-fluorobenzoyl/fluorobenzydryl)piperidines as potential CNS agents
AUTHOR(S): Tripathi, Ravish C.; Singh, H. K.; Saxena, Anil K.
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India

10/ 068,114

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1990), 29B(9), 865-9
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:6251
GI

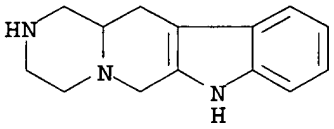


II

AB The key intermediate 1-(.gamma.-chloropropyl)-4-(4-fluorobenzoyl)piperidine has been prepd. by the condensation of 4-(4-fluorobenzoyl)piperidine (I) with 1-bromo-3-chloropropane. This on reaction with different amines, thiophenols and piperazines gives the title compds. II (R = sec-amine, thiolate). Compd. I on reaction with trans-2-phenoxymethylcyclopropane-1-carbonyl chloride yields trans-1-[4-(4-fluorobenzoyl)piperidin-1-ylcarbonyl]-2-phenoxymethylcyclopropane. Some of these compds. show potent CNS activity.

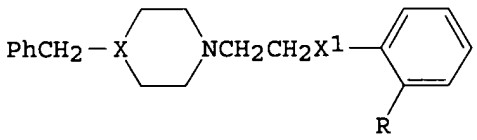
IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with (chloropropyl)(fluorobenzoyl)piperidine)

RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)

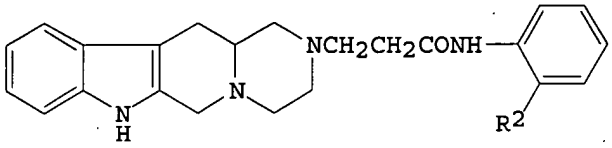


L4 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:611944 CAPLUS
DOCUMENT NUMBER: 113:211944
TITLE: Synthesis, biological evaluation, and quantitative structure-activity relationship analysis of [.beta.-(aroylamino)ethyl]piperazines and -piperidines and [2-[(arylamino)carbonyl]ethyl]piperazines, -piperidines, -pyrazinopyridoindoles, and -pyrazinoisoquinolines. A new class of potent H1 antagonists
AUTHOR(S): Saxena, Mridula; Agarwal, Shiv K.; Patnaik, G. K.; Saxena, Anil K.
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Journal of Medicinal Chemistry (1990), 33(11), 2970-6
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:211944
GI

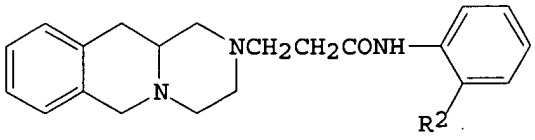
10/ 068,114



I



II



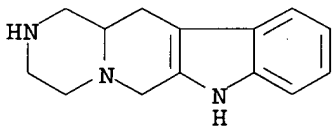
III

AB The title compds. I (R = H, Me, Et, Br, Cl, F, iodo, NO2; X = CH, N; X1 = CONH, NHCO), II and III (R2 = H, MeO, Et, Cl, F, NO2) were prepd. and their H1-antagonistic activity studied in isolated guinea pig ileum. Quant. structure-activity relationship anal. indicates that the hydrophobicity of the side chain of these compds. plays a major role in their activity while steric and electronic factors are of secondary importance. All acted on a common receptor and appear to interact similarly with the receptor.

IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with bromopropionamides)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:611942 CAPLUS

DOCUMENT NUMBER: 113:211942

TITLE: Synthesis and biological activities of trans-1-substituted-2(phenoxymethyl)cyclopropanes

AUTHOR(S): Tripathi, Ravish C.; Saxena, Anil K.; Anand, Nitya

CORPORATE SOURCE: Cent. Drug. Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1990), 29B(5), 455-8
CODEN: IJSBDB; ISSN: 0376-4699

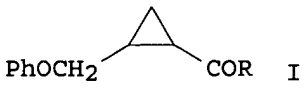
DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 113:211942

GI

10/ 068,114



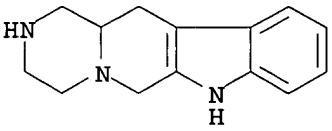
I

AB trans-2-Phenoxymethylcyclopropanecarboxylic acid chloride I (R = Cl) was reacted with amines to give the substitution products I (e.g., R = NHNH2, NHNHPh, NHC6H4OH-2, NHC6H3Cl2-2,6). Conversion of I (R = Cl) to the corresponding amine was also achieved in 3 steps. The prepd. compds. were tested for biol. activity. Some showed significant diuretic, antiinflammatory, and hypotensive activity.

IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reaction of, with (phenoxymethyl)cyclopropanecarboxylic acid)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1990:597746 CAPLUS

DOCUMENT NUMBER: 113:197746

TITLE: Analytical and shelf-life studies on centbutindole, a new neuroleptic compound

AUTHOR(S): Seth, R. K.; Sarin, J. P. S.

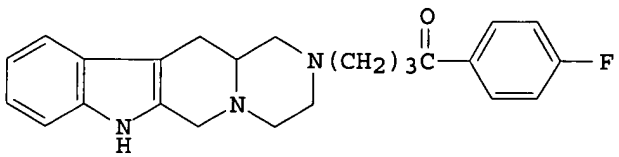
CORPORATE SOURCE: Div. Pharm., Cent. Drug Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Pharmaceutical Sciences (1989), 51(6), 244-7
CODEN: IJSIDW; ISSN: 0250-474X

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



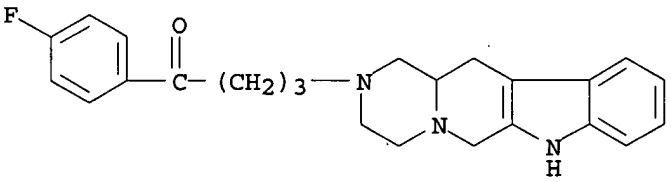
I

AB Centbutindole (I) was stable in pharmaceuticals (capsules, tablets, and injections) for 4 yr at room temp. No change in general appearance, TLC pattern, UV absorption pattern, and drug content was obsd. on heating I at 100.degree. for 6 h. A UV spectrophotometric method was convenient for the detn. of I in dosage forms.

IT **42021-34-1**, Centbutindole

10/ 068,114

RL: BIOL (Biological study)
(stability in pharmaceuticals of, UV spectrophotometric and TLC study of)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



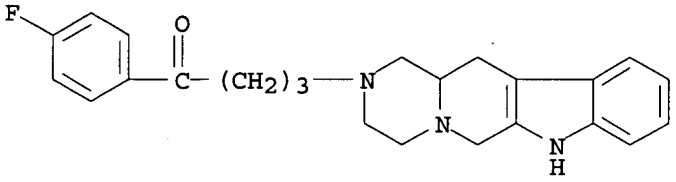
L4 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:545612 CAPLUS
DOCUMENT NUMBER: 113:145612
TITLE: Effect of melanotropin release inhibiting factor on changes by haloperidol and centbutindole in cerebral cortical 5-hydroxytryptamine receptors
AUTHOR(S): Gulati, Anil; Bhargava, Hemendra N.
CORPORATE SOURCE: Chicago Health Sci. Cent., Univ. illinois, Chicago, IL, 60612, USA
SOURCE: Pharmacology (1990), 41(2), 98-106
CODEN: PHMGBN; ISSN: 0031-7012
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of melanotropin release inhibiting factor (Pro-Leu-Gly-NH2, MIF) was detd. on changes induced by 2 neuroleptics, haloperidol and centbutindole, in cerebral cortical 5-HT receptors. Male Sprague-Dawley rats were injected daily i.p. with vehicle, haloperidol (1.0 mg/kg), or centbutindole (0.5 mg/kg), resp., for 21 days. On day 22, these 3 groups were further divided into 2 subgroups and injected with either vehicle or MIF (2.0 mg/kg, i.p.) daily for 3 days. [3H]-5-HT was used to study 5-HT1 receptors, and [3H]spiroperidol to label 5-HT2 receptors in the cerebral cortex. Chronic administration of haloperidol increased (39.7%) the maximal binding capacity (Bmax) of [3H]-5-HT binding to 5-HT1 receptors. Dissocn. const. (Kd) values did not change. Centbutindole had no effect on 5-HT1 receptors. MIF had no effect on 5-HT1 receptors, nor did it alter haloperidol-induced increases in the Bmax of [3H]-5-HT binding to 5-HT1 receptors. Chronic administration of centbutindole increased (61.1%) the Bmax of [3H]spiroperidol binding to 5-HT2 receptors. No change occurred in the Kd values. Chronic treatment with haloperidol had no effect on 5-HT2 receptor characteristics. MIF had no effect on 5-HT2 receptors or on the increase in 5-HT2 receptor d. induced by centbutindole. The behavioral syndrome induced by 5-HTP (50, 100, and 200 mg/kg, i.p.) was also measured in rats treated chronically with haloperidol or centbutindole. Haloperidol had no effect on the 5-HTP syndrome, whereas centbutindole stimulated by 24-45% the intensity of the syndrome. MIF had no effect on the 5-HTP syndrome, nor did it alter the increase induced by centbutindole. Evidently, haloperidol and centbutindole differentially affect cortical 5-HT1 and 5-HT2 receptors. MIF does not by itself affect 5-HT receptors, nor does it reverse the up-regulation of 5-HT receptors induced by haloperidol and centbutindole.

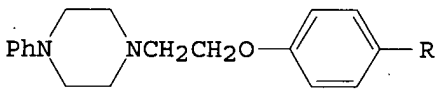
IT **42021-34-1**, Centbutindole
RL: BIOL (Biological study)
(serotonin receptor subtypes differential response to, in cerebral cortex, melanotropin release inhibiting factor action in relation to)

10/ 068,114

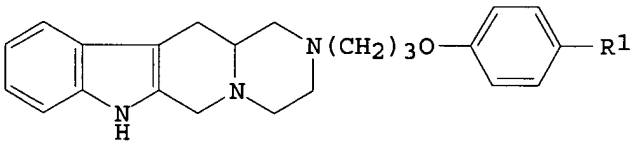
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



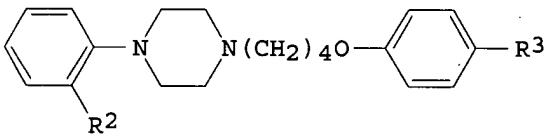
L4 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:235217 CAPLUS
DOCUMENT NUMBER: 112:235217
TITLE: Synthesis and structure-activity relationship in [(aryloxy)alkyl]amines
AUTHOR(S): Agarwal, Shiv K.; Saxena, Anil K.; Jain, Padam C.; Anand, Nitya; Sur, R. N.; Srimal, R. C.; Dhawan, Bhola N.
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1990), 29B(1), 80-4
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:235217
GI



I



II

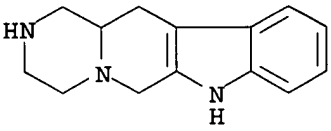


III

AB [(Aryloxy)alkyl]piperazine derivs. I (R = NO2, CHO, Br), II (R1 = NO2, F, NH2), and III (R2 = H, R3 = NO2, CHO, CH2OH; R2 = OMe, R3 = NO2, NH2) were prepd. and tested for central nervous system-depressant, antihistaminic, hypotensive, antiinflammatory, antiarrhythmic, diuretic, and anaphylaxis-inhibitory activity. All showed gross behavior-depressant activity and II (R = F) showed antihistaminic activity.
IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)

10/ 068,114

(substitution reaction of, with (aryloxy)chloropropanes)
RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)



L4 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:97553 CAPLUS
DOCUMENT NUMBER: 110:97553
TITLE: Organic solvent-soluble, oxide-supported hydrogenation catalyst precursors
INVENTOR(S): Edlund, David J.; Finke, Richard G.; Saxton, Robert J.
PATENT ASSIGNEE(S): University of Oregon, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8806489	A1	19880907	WO 1988-US609	19880226
W: AU, JP, NO, SU, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8814208	A1	19880926	AU 1988-14208	19880226
US 5116796	A	19920526	US 1988-275105	19881026
PRIORITY APPLN. INFO.:			US 1987-20122	19870227
			WO 1988-US609	19880226

OTHER SOURCE(S): MARPAT 110:97553
AB Catalyst precursors Ax(LnIr(I).X2M15M13O62]x- (A = countercation; L = olefinic ligand or dioxygen; M = W, Mo; M1 = Nb, V, Ti, Zr, Ta, Hf; X = B, Si, Ge, P, As, Se, Te, I, Co, Mn, Cu; n = 1, 2; x = .ltoreq.15), useful as precursors for the manuf. of org. solvent-sol. hydrogenation catalysts, are prepd. (Bu4N)8[(COD)Ir.P2W15Nb3O62].Bu4NBF4.9H2O (COD = 1,5-cyclooctadiene) was prepd. by adding a degassed soln. of (Bu4N)9P2W15Nb3O62 to a degassed acetonitrile soln. of [Ir(COD)(CH3CN)2]BF4.
IT **114672-71-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, in hydrogenation catalyst precursor manuf.)
RN 114672-71-8 CAPLUS
CN Niobate(9-), [heptacosa-.mu.-oxopentadecaoxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O'':O'':O''':O''']]pentadecatungstate]nona-.mu.-oxotrioxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O'':O'':O''':O''']]tri-, nonahydrogen, compd. with 2,3,4,6,7,8,9,10-octahydropyrazino[1,2-a]azepine (1:9), undecahydrate (9CI) (CA INDEX NAME)

CM 1

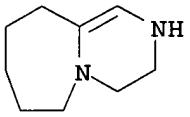
CRN 114672-70-7
CMF H . 1/9 Nb3 O62 P2 W15
CCI CCS

10/ 068,114

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 114672-69-4
CMF C9 H16 N2



L4 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:493246 CAPLUS
DOCUMENT NUMBER: 109:93246
TITLE: Trisubstituted heteropolytungstates as soluble metal oxide analogues. 4. The synthesis and characterization of organic solvent-soluble (Bu4N)12H4P4W30Nb6O123 and (Bu4N)9P2W15Nb3O62 and solution spectroscopic and other evidence for the supported organometallic derivatives (Bu4N)7[(C5Me5)Rh.cntdot.P2W15Nb3O62] and (Bu4N)7[(C6H6)Ru.cntdot.P2W15Nb3O62]
AUTHOR(S): Edlund, David J.; Saxton, Robert J.; Lyon, David K.; Finke, Richard G.
CORPORATE SOURCE: Dep. Chem., Univ. Oregon, Eugene, OR, 97403, USA
SOURCE: Organometallics (1988), 7(8), 1692-704
CODEN: ORGND7; ISSN: 0276-7333
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:93246
AB The synthesis and characterization of the previously unknown triniobium-substituted Dawson heteropolyanion, P2W15Nb3O629-, as its org. solvent sol. Bu4N+ salt, are described. The monomer P2W15Nb3O629- undergoes formation of a previously unknown Nb-O-Nb bridged species: 2P2W15Nb3O629- + 2H+ .dblharw. H2O + P4W30Nb6O12316-. The initial synthesis, at pH 4.6, yields the Me4N+ salt of this aggregate, (Me4N)12H4P4W30Nb6O123. Metathesis with Bu4N+ provides the Bu4N+ salt, (Bu4N)12H4P4W30Nb6O123. Cleavage/deprotonation of the latter salt with 6 equiv of Bu4NOH yields (Bu4N)9P2W15Nb3O62, which has been shown to form covalently attached, polyoxoanion-supported (C5Me5)Rh2+ and (C6H6)Ru2+ complexes of C3v symmetry in acetonitrile soln. by IR, 1H NMR, 31P NMR, and 183W NMR spectroscopy, soln. mol. wt. measurements, and tests with ion-exchange resins.
IT **114672-71-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 114672-71-8 CAPLUS
CN Niobate(9-), [heptacosa-.mu.-oxopentadecaoxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O'':O'':O''':O''']]pentadecatungstate]nona-.mu.-oxotrioxo[.mu.9-[phosphato(3-)-O:O:O:O':O':O'':O'':O''':O''']]tri-, nonahydrogen, compd. with 2,3,4,6,7,8,9,10-octahydropyrazino[1,2-a]azepine (1:9), undecahydrate (9CI) (CA INDEX NAME)

CM 1

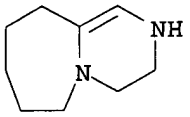
CRN 114672-70-7
CMF H . 1/9 Nb3 O62 P2 W15
CCI CCS

10/ 068,114

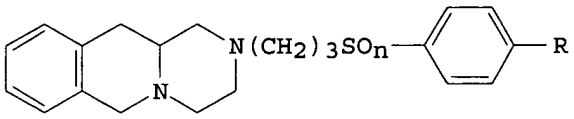
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 114672-69-4
CMF C9 H16 N2



L4 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:422938 CAPLUS
DOCUMENT NUMBER: 109:22938
TITLE: Synthesis of N-[3-aryl(thio/sulfono)propyl]heterocyclics as potential CNS/CVS agents
AUTHOR(S): Rao, Jyoti; Saxena, Anil K.; Saxena, R. M.; Singh, H. K.; Kar, K.; Srimal, R. C.
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1987), 26B(8), 761-5
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:22938
GI

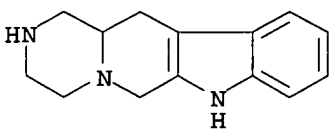


I

AB Condensation of 4-RC6H4SOn(CH2)3Cl (n = O, R = NHAc, OMe, Me; n = 2, R = NHAc) with 1-benzylpiperazine, 4-benzylpiperidine, octahydropyrazinoisoquinoline, and octahydropyrazinopyridoindole gave the corresponding adducts, e.g., I, in 44-83% yields. Hydrolysis of the acetamido derivs. gave the corresponding amino derivs., e.g. I (n = O, R = NH2, II). Reductive methylation of II gave I (R = NMe2). These compds. exhibit good hypotensive, antiinflammatory, diuretic, anxiolytic and passive cutaneous anaphylaxis activities.

IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of, with arylthio- and arylsulfonyl chlorides)

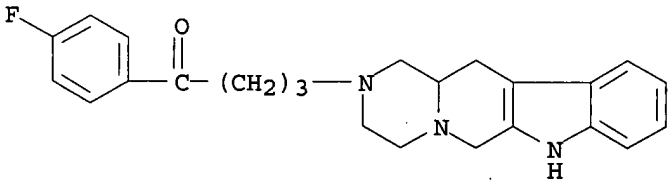
RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1988:400681 CAPLUS
DOCUMENT NUMBER: 109:681
TITLE: Differential alteration in striatal dopaminergic and cortical serotonergic receptors induced by repeated administration of haloperidol or centbutindole in rats
AUTHOR(S): Gulati, Amir; Srimal, R. C.; Dhawan, B. N.
CORPORATE SOURCE: Coll. Pharm., Univ. Illinois, Chicago, IL, 60612, USA
SOURCE: Pharmacology (1988), 36(6), 396-404
CODEN: PHMGBN; ISSN: 0031-7012
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Centbutindole is a new neuroleptic drug having a pharmacol. profile similar to haloperidol, but it does not cause hypothermia and has a higher sepn. between doses causing catalepsy and neurolepsy. The interactions of centbutindole with striatal dopamine and cortical 5-HT2 receptors have been studied along with haloperidol. Rats received haloperidol (1.0 mg/kg, p.o.), centbutindole (0.5 mg/kg, p.o.) or saline daily for 21 days. Following drug withdrawal for 3 days, apomorphine (0.1-1.0 mg/kg, i.p.) or 5-hydroxytryptamine (5-HTP, 50-200 mg/kg, i.p.) was injected. Apomorphine-induced stereotyped behavior was potentiated in the haloperidol-treated rats, while the 5-HTP-induced behavioral syndrome was increased in centbutindole-treated rats. Receptor binding studies indicated an increase in the maximal binding capacity Bmax of striatal dopamine receptor (29.4%) in haloperidol-treated and of cortical 5-HT2 receptor (17.8%) in centbuindole-treated animals. No change in the apparent dissocn. const. Kd was obsd. Repeated treatment with haloperidol produced striatal dopamine receptor supersensitivity, while centbutindole treatment produced cortical serotonergic receptor supersensitivity.

IT **42021-34-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dopaminergic and serotoninergic receptors of brain response to)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



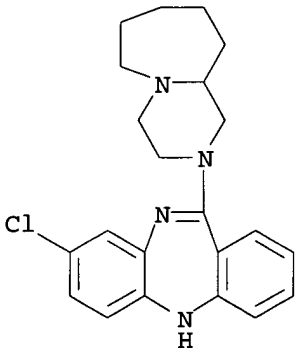
L4 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:617657 CAPLUS
DOCUMENT NUMBER: 107:217657
TITLE: 11-[N-(Diazabicyclo[4.m.0]alkanyl)]-5H-dibenzo[b,e][1,4]diazepines with neuroleptic activity
INVENTOR(S): Likhosherstov, A. M.; Raevskii, K. S.; Stavrovskaya, A. V.; Skoldinov, A. P.; Rostock, Angelika; Rueger, Carla; Roehnert, Helmut
PATENT ASSIGNEE(S): Scientific-Research Institute of Pharmacology, Academy of Medical Sciences, U.S.S.R., USSR; VEB Arzneimittelwerk Dresden
SOURCE: U.S.S.R. From: Otkrytiya, Izobret. 1986, (46), 296.

10/ 068,114

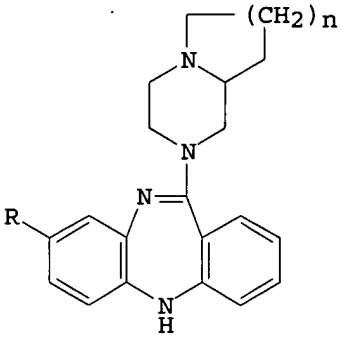
CODEN: URXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
SU 1015618	A1	19861215	SU 1980-2923128	19800128

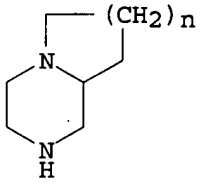
PRIORITY APPLN. INFO.: SU 1980-2923128 19800128
GI For diagram(s), see printed CA Issue.
AB The title compds. (I; R = H, m = 3; R = Cl, m = 3-5) have neuroleptic activity (no data).
IT **81469-87-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(neuroleptic activity of)
RN 81469-87-6 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1985:220842 CAPLUS
DOCUMENT NUMBER: 102:220842
TITLE: Synthesis and neuroleptic effects of new 11-substituted 5H-dibenzo[b,e][1,4]diazepines
AUTHOR(S): Skoldinov, A. P.; Raevskii, K. S.; Likhosherstov, A. M.; Stavrovskaya, A. V.; Rueger, Carla; Rostock, Angelika; Roehnert, H.
CORPORATE SOURCE: Inst. Pharmacol. Med. Sci., Moscow, 125315, USSR
SOURCE: Pharmazie (1984), 39(12), 812-13
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 102:220842
GI



I



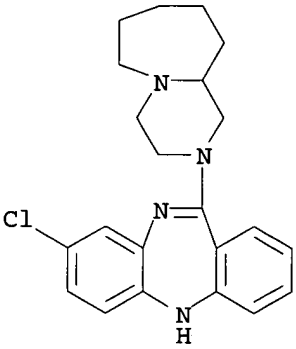
II

AB The title compds. (I; R = H, n = 1; R = Cl, n = 1-3), prepd. in 42.0-64.4% yield by treating a dibenzodiazepinone with a perhydro fused-ring pyrazine (II) in the presence of TiCl4, were tested for neuroleptic activity. I (R = Cl, n = 1) was the most effective in these tests.

IT **81469-87-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and neuroleptic activity of)

RN 81469-87-6 CAPLUS

CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)- (9CI) (CA INDEX NAME)



IT **81469-88-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

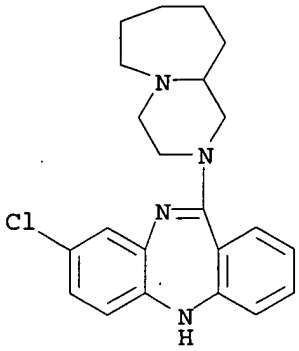
RN 81469-88-7 CAPLUS

CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 81469-87-6
CMF C22 H25 Cl N4

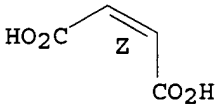
10/ 068,114



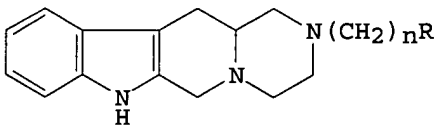
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



L4 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:455059 CAPLUS
DOCUMENT NUMBER: 101:55059
TITLE: Synthesis and QSAR in 2-substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indoles - a new class of H1-antagonists
AUTHOR(S): Saxena, Anil K.; Dhaon, Madhup K.; Ram, Siya; Saxena, Mridula; Jain, Padam; Patnaik, G. K.; Anand, Nitya
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1983), 22B(12), 1224-32
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



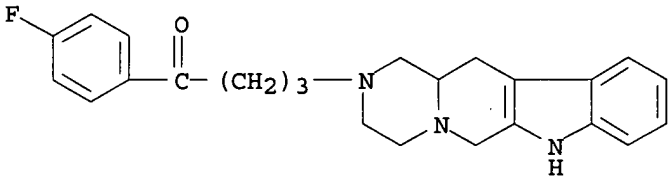
I

AB Pyrazinopyridoindoles I [R = (un)substituted PhCONH, Ph2CHO, etc.; n = 2, 3] were prepd. and tested for their H1-receptor antagonistic action in guinea pig ileum. The quant. structure-activity anal. of 34 compds. showed that the activity is influenced by hydrophobicity of the side chain and by the bulk of the substituent at the ortho-position of the Ph ring of the .beta.-aroylaminoethyl side chain. Comparing these results with those of diphenylhydramine suggests that the Ph ring of the side chain and N2 of

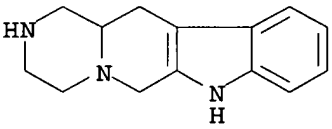
10/ 068,114

I (R = PhCONH, n = 2) could occupy the same receptor sites as 1 of the Ph rings of diphenylhydramine and its tertiary N.

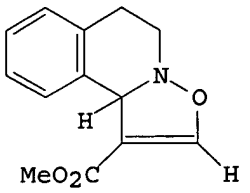
IT **42021-34-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Grignard reaction of, with Me iodide)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



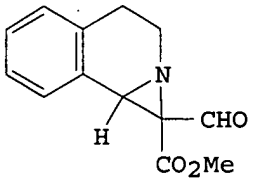
IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyanoalkylation of)
RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



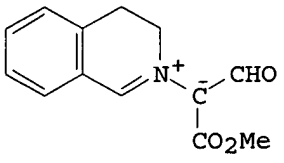
L4 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:174024 CAPLUS
DOCUMENT NUMBER: 100:174024
TITLE: The chemistry of an isolable azomethine ylide
AUTHOR(S): Huisgen, Rolf; Niklas, Karl
CORPORATE SOURCE: Inst. Org. Chem., Univ. Muenchen, Munich, D-8000/2, Fed. Rep. Ger.
SOURCE: Heterocycles (1984), 22(1), 21-6
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 100:174024
GI



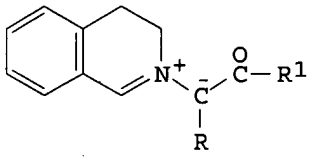
I



II



III



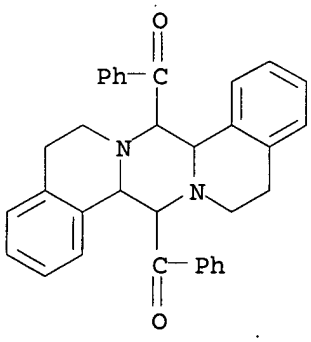
IV

AB The 4-isoxazoline I undergoes ring contraction to the acylaziridine II which is converted to the azomethine ylide III. The small influence of solvent polarity on the rate const. of the conversion I .fwdarw. III suggests a mechanism via a trimethylene type species for the rate-detg. step. Whereas III is the first azomethine ylide which can be isolated without being stabilized by arom. resonance, the ylides IV (R = H, CO2N; R1 = Me, Ph) dimerize to piperazine derivs. 1,3-Dipolar cycloaddns. of the azomethine ylides III and IV are described.

IT **89768-86-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 89768-86-5 CAPLUS

CN Methanone, (5,6,8,8a,13,14,16,16a-octahydropyrazino[2,1-a:5,4-a']diisoquinoline-8,16-diyl)bis[phenyl- (9CI) (CA INDEX NAME)



L4 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1984:34500 CAPLUS

DOCUMENT NUMBER: 100:34500

TITLE: Studies in potential filaricides: Part XIII-Synthesis of 1,4-diazabicyclo[4.3.0]nonanes, 1,4-diazabicyclo[4.4.0]decanes and 1,4-diazabicyclo[4.5.0]undecanes as diethylcarbamazine analogs

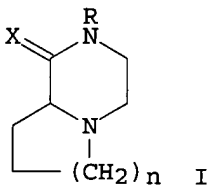
AUTHOR(S): Shukla, U. K.; Khanna, J. M.; Sharma, Satyavan; Anand, Nitya; Chatterjee, R. K.; Sen, A. B.

CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow, 226 001, India

SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1983),

10/ 068,114

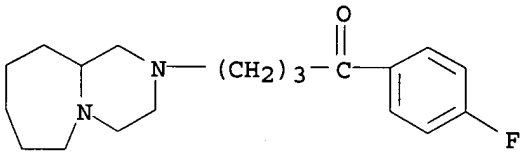
22B(7), 664-8
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 100:34500
GI



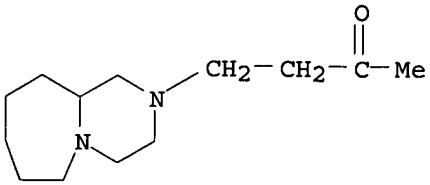
AB The title compds. I [n = 1-3; X = H2, O; R = (un)substituted alkyl, CONEt2] were prepd. and evaluated for their filaricidal activity against Litomosoides carinii infection in cotton rats. Except I (n = 1, R =CONEt2, X = H2) which is .apprx.60% as active as the std. diethylcarbamazine (II), none of the other compds. shows any activity against adult worms. The results have been rationalized in terms of crit. bulk around N-1 of the piperazine ring of II. It appears that both axial and equatorial N-Me bonds in II are acceptable for activity.

IT **60390-52-5P 88327-82-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and filaricidal activity of)

RN 60390-52-5 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)- (9CI) (CA INDEX NAME)



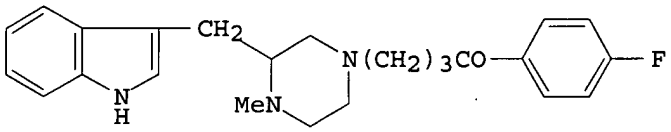
RN 88327-82-6 CAPLUS
CN 2-Butanone, 4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)- (9CI) (CA INDEX NAME)



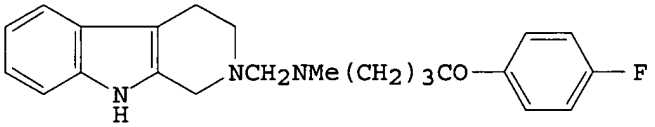
L4 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1983:16659 CAPLUS
DOCUMENT NUMBER: 98:16659
TITLE: Agents acting on CNS. Part XXIX. Synthesis of seco analogs of centbutindole, a potent neuroleptic.
AUTHOR(S): Kumar, Naresh; Dhaon, Madhup K.; Agarwal, Shiv K.;

10/ 068,114

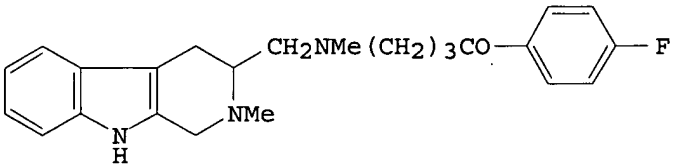
Saxena, Anil K.; Jain, Padam C.; Prasad, C. R.; Anand, Nitya
CORPORATE SOURCE: Div. Med. Chem. Pharmacol. Div., Cent. Drug Res. Inst., Lucknow, 226001, India
SOURCE: European Journal of Medicinal Chemistry (1982), 17(4), 312-16
CODEN: EJMCA5; ISSN: 0009-4374
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 98:16659
GI



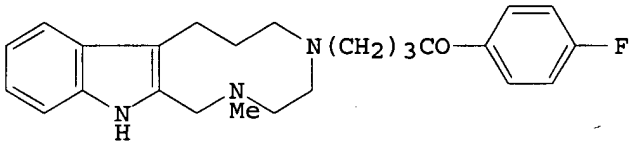
I



II



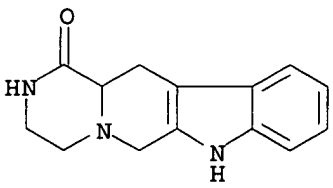
III



IV

AB Four seco analogs of centbutindole I, II, III, and IV were prepd. and their tranquilizing activities detd. The reduced activities of I-IV confirm that the rigid conformations of tryptamine and piperazine moieties are essential for this activity.

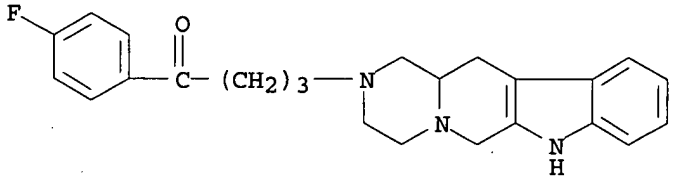
IT **55344-27-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and quaternization of, by Me iodide)
RN 55344-27-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



IT **42021-34-1DP**, seco analogs

10/ 068,114

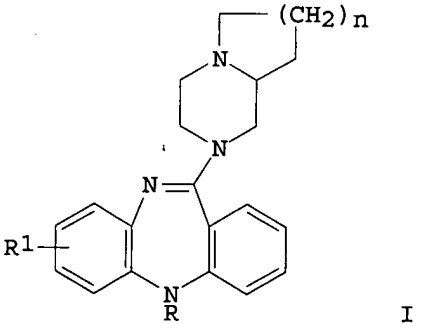
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1982:162757 CAPLUS
DOCUMENT NUMBER: 96:162757
TITLE: 5H-Dibenzo[b,e][1,4]diazepines substituted in the 11-position
INVENTOR(S): Rueger, Carla; Rostock, Angelika; Roehnert, Helmut; Skoldinov, A. P.; Raevskii, K. S.; Likhosherstov, A. M.; Stavrovskaya, A. V.
PATENT ASSIGNEE(S): Ger. Dem. Rep.
SOURCE: Ger. (East), 30 pp.
CODEN: GEXXA8
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 151166	Z	19811008	DD 1979-216678	19791105

PRIORITY APPLN. INFO.: DD 1979-216678 19791105
GI

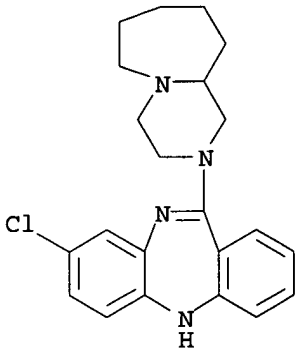


I

AB Dibenzazepines I (R = H, Me; R1 = H, Cl; n = 1-3) were prepd. Thus 8-chloro-10,11-dihydro-11-oxo-5H-dibenzo[b,e][1,4]diazepine was treated with octahydropyrrolo[1,2-a]pyrazine to give 58% I (R = H, R1 = 8-Cl, n = 1) which had a spontaneous motility-inhibiting ED50 of 3.9 mg/kg in mice.
IT **81469-87-6P 81469-88-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

10/ 068,114

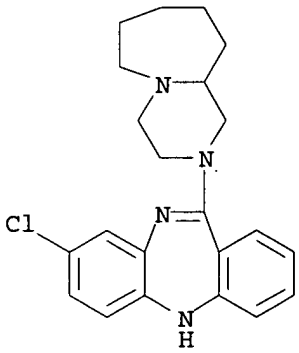
RN 81469-87-6 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)- (9CI) (CA INDEX NAME)



RN 81469-88-7 CAPLUS
CN 5H-Dibenzo[b,e][1,4]diazepine, 8-chloro-11-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

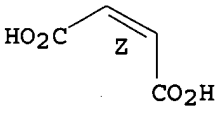
CRN 81469-87-6
CMF C22 H25 Cl N4



CM 2

CRN 110-16-7
CMF C4 H4 O4

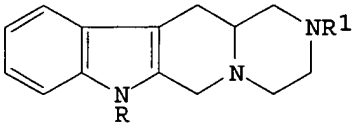
Double bond geometry as shown.



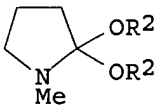
L4 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:532811 CAPLUS
DOCUMENT NUMBER: 95:132811
TITLE: A convenient method for indole N-alkylation in substituted pyrazino[2,1:6,1]pyrido[3,4-b]indoles

10/ 068,114

AUTHOR(S): Agarwal, Shiv K.; Saxena, Anil K.; Anand, Nitya
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, 226001, India
SOURCE: Synthesis (1981), (6), 465-6
CODEN: SYNTBF; ISSN: 0039-7881
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

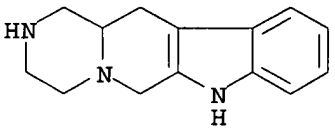


II

AB Treatment of pyrazinopyridoindoles I [R = H; R1 = PhCH2, 2-(4-pyridyl)ethyl, 4-FC6H4CO(CH2)3, 4-ClC6H4CONHCH2CH2] with dialkoxypyrrolidines II (R2 = Me, Et, Pr) in THF at 35.degree. for 6 h gave 72-90% I (R = Me, Et, Pr; R1 as above).

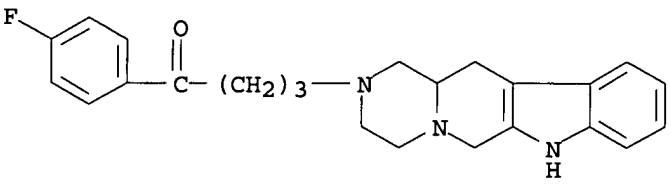
IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzylation of)

RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



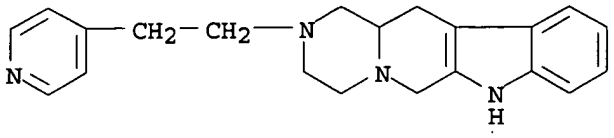
IT **42021-34-1P 55344-34-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of, by dialkoxypyrrolidines)

RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

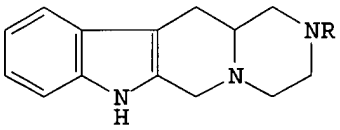


RN 55344-34-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

10/ 068,114



L4 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1981:208809 CAPLUS
DOCUMENT NUMBER: 94:208809
TITLE: Agents acting on CNS. Part XXX. Synthesis of 2-substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2'1':6,1]pyrido[3,4b]indoles
AUTHOR(S): Dhaon, Madhup K.; Kumar, Naresh; Agarwal, Shiv K.; Saxena, Anil K.; Jain, Padam C.; Anand, Nitya
CORPORATE SOURCE: Cent. Drug Res. Inst., Lucknow, 226 001, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1980), 19B(10), 882-5
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

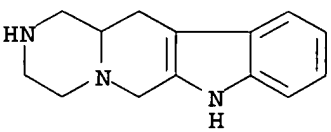


I

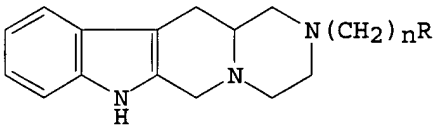
AB 2-Substituted pyrazinopyridoindoles I [R = p-ClC6H4CO, p-FC6H4CMe(OH)(CH2)3, Ph2C:CHCH2, etc.] were prepd. by the condensation of I (R = H) with the appropriate halogen compds. Treatment of I (R = H) with ethylene oxide gives I (R = HOCH2CH2) which on condensation with p-fluorobenzoyl chloride yields I (R = p-FC6H4CO2CH2CH2). The corresponding 2-.gamma.-(p-fluorobenzoyl)propyl-6-oxooctahydropyrazinopyridoindole is prepd. by the oxidn. of I (R = H) with mercuric acetate followed by condensation of the resulting 6-oxo deriv. with .gamma.-chloro-p-fluorobutyrophenone. 2-Substituted-1-oxopyrazinopyridoindoles are prepd. by the reaction of ethylene oxide with Me 1,2,3,4-tetrahydropyrido[3,4-b]indole-3-carboxylate followed by condensation of the resulting oxazino deriv. with amines. These compds. show tranquilizing, antiinflammatory, and diuretic activities.

IT **55344-28-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(substitution reactions of)

RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:69309 CAPLUS
DOCUMENT NUMBER: 92:69309
TITLE: Antihistaminic activity of 2-substituted pyrazinopyridoindoles
AUTHOR(S): Patnaik, G. K.; Jain, P. C.; Das, P. K.; Dhawan, B. N.
CORPORATE SOURCE: Dep. Pharmacol., Inst. Med. Sci., Lucknow, India
SOURCE: Indian Journal of Pharmacology (1979), 11(2), 139-42
CODEN: INJPD2; ISSN: 0253-7613
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

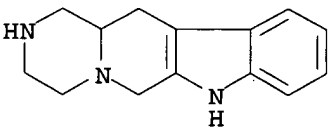


I

AB The relative antihistaminic activities of 39 pyrazinopyridoindoles I (R = substituted benzamido, OCHPhC6H4F-4, etc; n = 2 or 3) were tested in isolated guinea pig ileum prepns. and were related to structure. All of the compds. selectively blocked the response of the ileum to histamine-2HCl without affecting acetylcholine chloride-induced spasms. Even the most active of the derivs. were 10-fold less effective than the ref. std. diphenhydroamine.

IT **55344-28-0D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antihistaminic activity of, structure in relation to)

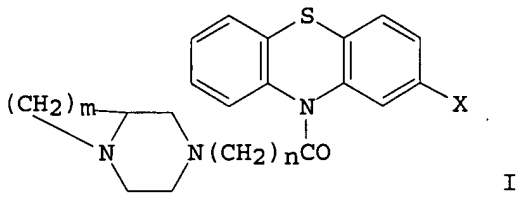
RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1978:590804 CAPLUS
DOCUMENT NUMBER: 89:190804
TITLE: Azacycloalkanes. XXI. Relation between the structure and the antianginal properties in a series of 1,4-diazabicyclo[4.m.0]alkanyl derivatives of 10-acylphenothiazines
AUTHOR(S): Nazarova, L. S.; Likhosherstov, A. M.; Markova, G. A.; Chichkanov, G. G.; Kaverina, N. V.; Skoldinov, A. P.
CORPORATE SOURCE: Inst. Farmakol., Moscow, USSR
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1978), 12(6), 84-9
CODEN: KHFZAN; ISSN: 0023-1134
DOCUMENT TYPE: Journal
LANGUAGE: Russian

10/ 068,114

GI



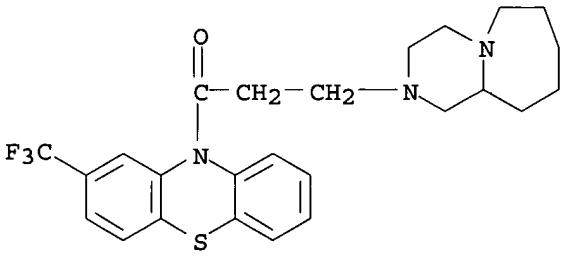
I

AB The title compds (I) (n = 1,2, or 3; m = 3 or 5; X = H, Cl, or CF3) were prepd. by condensation of 1,4-diazobicyclo[4.m.0]alkanes with 10-(.omega.-chloroacyl)phenothiazines and studied for their effects on coronary blood flow and myocardial function in cats. Lengthening of the acyl group increased coronary blood flow and increased myocardial contraction without the development of tachycardia. Trichloromethyl substitution at position 2 of the phenothiazine system increased the duration of coronary blood flow effects. The 1,4-diazabicyclo[4.5.0] derivs. were less active than the 1,4-diazabicyclo[4.3.0] derivs. The most promising antianginal compds. were 10-[.beta.-N-(1,4-diazabicyclo[4.3.0]nonaryl)propionyl]-2-chlorophenothiazine dihydrochloride [49780-10-1] and 10-[.beta.-N-(1,4-diazabicyclo[4.3.0]nonanyl)propionyl]-2-trifluoromethylphenothiazine dihydrochloride [49780-09-8].

IT **49780-15-6 68027-97-4**
RL: BIOL (Biological study)
(antianginal properties of, structure in relation to)

RN 49780-15-6 CAPLUS

CN 10H-Phenothiazine, 10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-2-(trifluoromethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

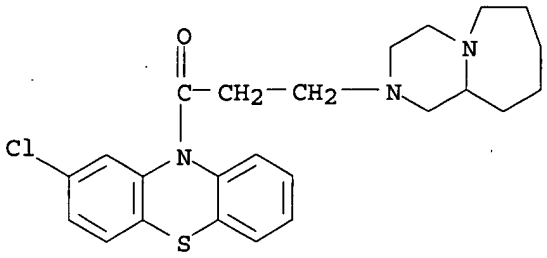


●2 HCl

RN 68027-97-4 CAPLUS

CN 10H-Phenothiazine, 2-chloro-10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-, dihydrochloride (9CI) (CA INDEX NAME)

10/ 068,114

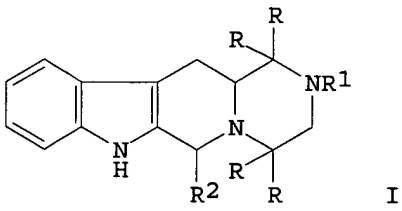


●2 HCl

L4 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1977:171497 CAPLUS
DOCUMENT NUMBER: 86:171497
TITLE: Tetracyclic compounds
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India
SOURCE: Brit., 9 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1454171	A	19761027	GB 1973-44002	19731019

PRIORITY APPLN. INFO.: GB 1973-44002 19731019
GI

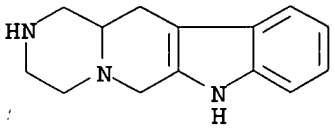


I

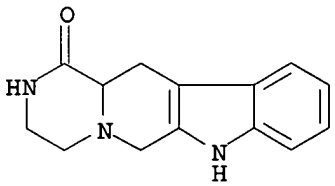
AB Thirty-one 2-substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-b]indoles I [R = H, R2 = O; R1 = aroylalkyl, arylhydroxyalkyl, hydroxyalkyl, oxoalkyl. aminoalkyl, Me, PhCH2CO, Ph(CH2)2, benzodioxanylmethyl, PhOCH(OH)CH2, NC(CH2)2, HO2C(CH2)2, EtO2C(CH2)2; R2 = H, Me] were prepd. from alkyl 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylates by 2 main methods. The 1st involved successive acid-catalyzed condensation with ethylenimine (II), (if necessary) LiAlH4 redn., and introduction of 2-substituents. The 2nd involved successive treatment with haloacetyl halides and primary amines. Thus, I [R = R2 = H, R1 = p-FC6H4CO(CH2)3] (III) was prepd. from Me 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylate (IV) by refluxing with IV.HCl and II in EtOH 48 h followed by LiAlH4 redn. in THF and treatment with p-FC6H4CO(CH2)3Cl in DMF contg. Na2CO3 and NaI 36 h at 80.degree.. I show strong tranquilizing and hypotensive activity. Animal tests on III are reported; III had LD50 values in mice of 180 mg/kg i.p. and >1 g orally. III also shows antiemetic activity.

10/ 068,114

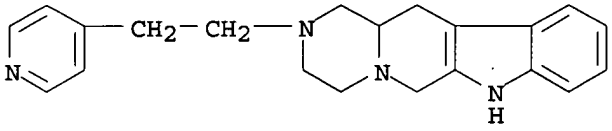
IT **55344-28-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of)
RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI). (CA INDEX NAME)



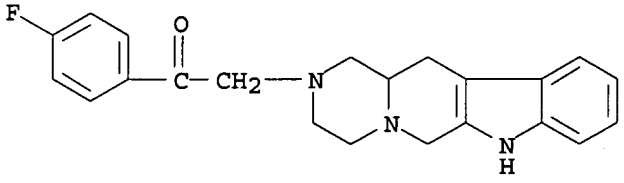
IT **55344-27-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 55344-27-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



IT **55344-34-8P 55344-36-0P 55344-50-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(tranquilizers and hypotensive agent, prepn. of)
RN 55344-34-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

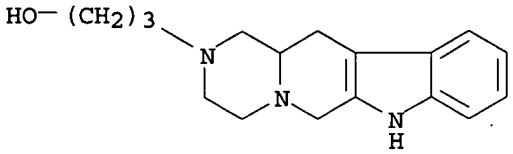


RN 55344-36-0 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

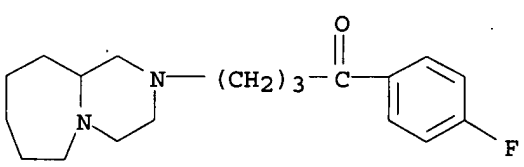


10/ 068,114

RN 55344-50-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



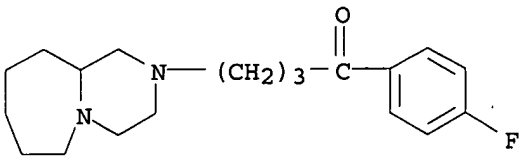
L4 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:508620 CAPLUS
DOCUMENT NUMBER: 85:108620
TITLE: Azacycloalkanes. XV. Relation between the structure and neurotropic activity in a series of 1,4-diazabicyclo[4.m.0]alkanyl derivatives of butyrophenone
AUTHOR(S): Nazarova, L. S.; Likhosherstov, A. M.; Raevskii, K. S.; Breger, M. A.; Skoldinov, A. P.
CORPORATE SOURCE: Inst. Farmakol., Moscow, USSR
SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1976), 10(4), 49-55
CODEN: KHFZAN; ISSN: 0023-1134
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Five diazabicycloalkanes I (m = 3, 4, 5; X = F, Cl, H) were prepd. in 31-62.9% yield by reaction of the corresponding diazabicyclalkanes with X1(CH2)3COC6H4X-p (X1 = Cl, Br); the dihydrochlorides were also prepd. Redn. of I (m = 3; X = F) gave 74% resp. alc. Reaction of 1,4-diazabicyclo[4.3.0]nonane-4-ethanol with p-XC6H4COCl (X = H, F) gave the corresponding II in 58.7 and 38% yield, resp. 1,4-Diazabicyclo[4.3.0]nonane-4-butyric acid was prepd. in 66.5% yield by hydrolysis of the Et ester. I (m = 4, X = F) increased the duration of the narcotic effect of sodium thiopental and was more active than I (m = 3, 5, X = F). When X = F the compds. had a stronger neuroleptic effect than when X = Cl, H. The CO played an important role in neuroleptic activity.
IT **60390-52-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and neurotropic activity of)
RN 60390-52-5 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)- (9CI) (CA INDEX NAME)



IT **60417-35-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 60417-35-8 CAPLUS

10/ 068,114

CN 1-Butanone, 1-(4-fluorophenyl)-4-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-, dihydrochloride (9CI) (CA INDEX NAME)

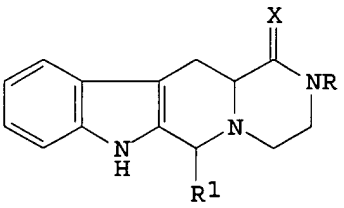


●2 HCl

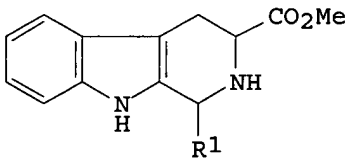
L4 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:405673 CAPLUS
DOCUMENT NUMBER: 85:5673
TITLE: 2-Substituted-1,2,3,4,6,7,12,12a-octahydropyrazino-[2',1':6,1]pyrido[3,4-b]indoles
INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Dua, Prithvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya; Singh, Gurbuksh
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India
SOURCE: Can., 25 pp.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 982132	A1	19760120	CA 1973-172016	19730523

PRIORITY APPLN. INFO.: CA 1973-172016 19730523
GI



I



II

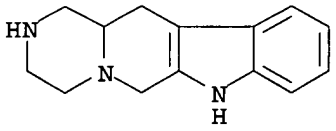
AB About 30 pyrazinopyridoindoles I (R = H, p-FC6H4CO(CH2)3, Me, 2-(4-pyridyl)ethyl, Et2NCH2CH2, PhCH2CO, EtO2CCH2CH2, MeCOCH2CH2, etc.; R1 = H, Me; X = H2) were prepd. from II. Thus II (R1 = H) was treated with ethylenimine and the I (R = R1 = H, X = O) reduced with LiAlH4 to give I (R = R1 = H, X = H2), which was treated with Cl(CH2)3COC6H4F-p to give I [R = p-FC6H4CO(CH2)3, R1 = H, X = H2] (III). The depressant ED50 of III was 0.5 mg/kg in the amphetamine hyperactivity test (i.p. mice).

IT **55344-28-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of)

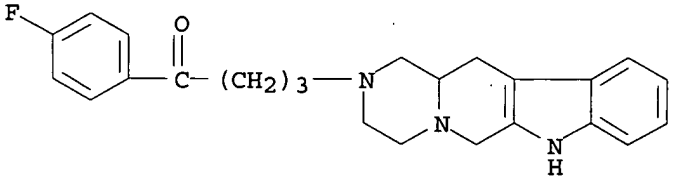
RN 55344-28-0 CAPLUS

10/ 068,114

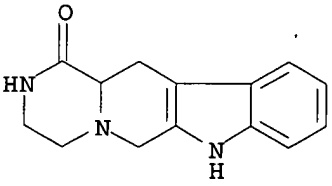
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



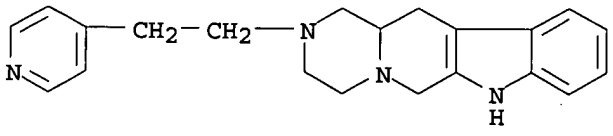
IT **42021-34-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and depressant activity of)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



IT **55344-27-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 55344-27-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)

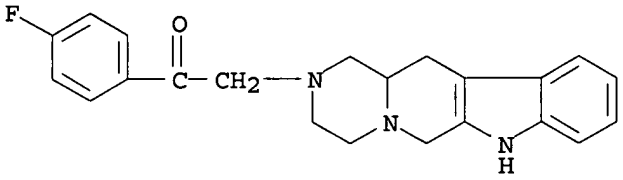


IT **55344-34-8P 55344-36-0P 55344-50-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 55344-34-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

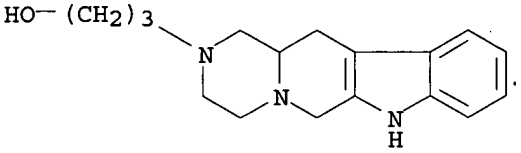


10/ 068,114

RN 55344-36-0 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



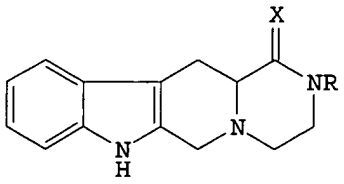
RN 55344-50-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:164842 CAPLUS
DOCUMENT NUMBER: 84:164842
TITLE: 2-Substituted-1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indoles
INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Singh, Gurbuksh; Dua, Prithvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India), India
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3917599	A	19751104	US 1973-346468	19730330

PRIORITY APPLN. INFO.: US 1973-346468 19730330
GI



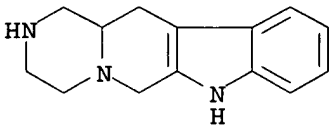
I

AB Me 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylate was cyclized with ethylenimine to give the pyrazinopyridoindole I (R = H, X = O), which was reduced and alkylated to give I (R = Me. PhCH2CO, p-FC6H4CO(CH2)3, 4-pyridylethyl, etc., X = H2). At 2.5-35 mg/kg I [R = p-FC6H4CO(CH2)3, X = H2] (II) reduced spontaneous motor activity of mice in several tests. The LD50 of II was 180 mg/kg, i.p. in mice.

IT **55344-28-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and alkylation of)

RN 55344-28-0 CAPLUS

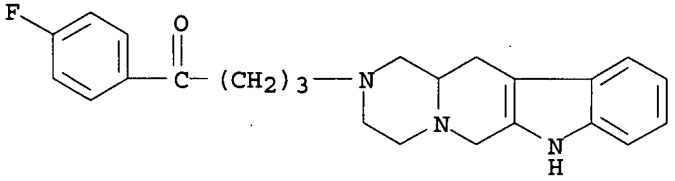
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



IT **42021-34-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and depressant activity of)

RN 42021-34-1 CAPLUS

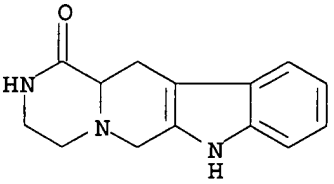
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



IT **55344-27-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)

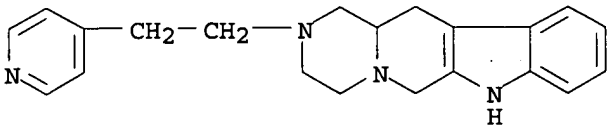


IT **55344-34-8P 55344-36-0P 55344-50-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

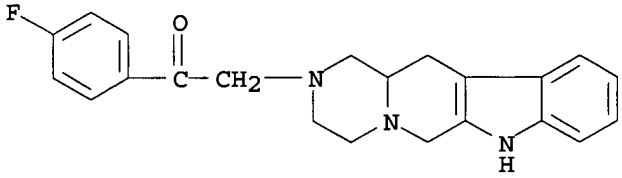
RN 55344-34-8 CAPLUS

10/ 068,114

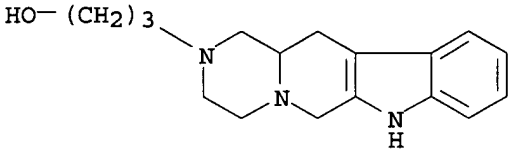
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 55344-36-0 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



RN 55344-50-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



L4 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:171057 CAPLUS
DOCUMENT NUMBER: 82:171057
TITLE: 1,2,3,4,6,7,12,12a-Octahydropyrazino[2,1:6,1]pyrido[3,4-b]indole depressants
INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Singh, Gurbukhsh; Dua, Prithvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya
PATENT ASSIGNEE(S): Gruppo Lepetit S.p.A.
SOURCE: Fr. Demande, 16 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2223013	A1	19741025	FR 1974-9968	19740322
FR 2223013	B1	19770701		
SE 408710	C	19791011	SE 1973-14117	19731017
SE 408710	B	19790702		
AU 7361649	A1	19750424	AU 1973-61649	19731022

NL 171270	B	19821001	NL 1973-15803	19731119
NL 171270	C	19830301		
CH 596205	A	19780315	CH 1973-16535	19731123
DK 141702	B	19800527	DK 1974-1712	19740328
DK 141702	C	19801027		

PRIORITY APPLN. INFO.: US 1973-346408 19730330

GI For diagram(s), see printed CA Issue.

AB Pyrazinopyridoindoles I (R = oxoalkyl, hydroxyalkyl, aminoalkyl etc; X = H2, O; R1 = H, Me) (34 compds.) were prepd. for use as central nervous system depressants. Thus Me 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylate was treated with ethylenimine and reduced with LiAlH4 to give I (X = H2, R = R2 = H), which was treated with p-FC6H4CO(CH2)3Cl to give I (X = H2, R = (CH2)3COC6H4F-4, R1 = H). The latter compd. had a ED50 in the Rotarod test in mice of 5.9 mg/kg i.p.

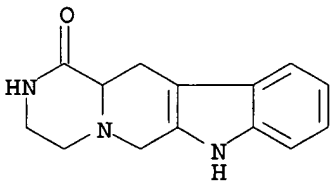
IT **55344-27-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and redn. of)

RN 55344-27-9 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



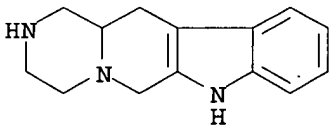
IT **55344-28-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and substitution reactions of)

RN 55344-28-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



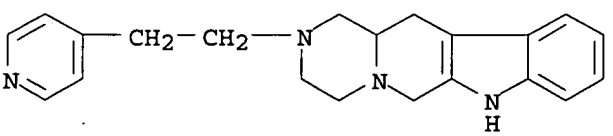
IT **55344-34-8P 55344-36-0P 55344-50-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

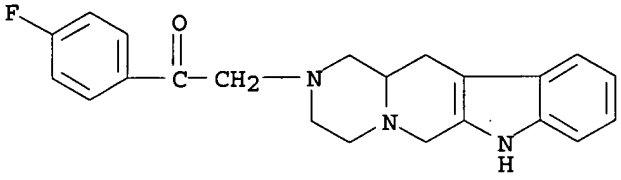
RN 55344-34-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

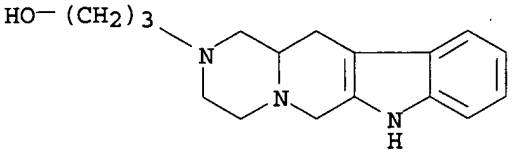


10/ 068,114

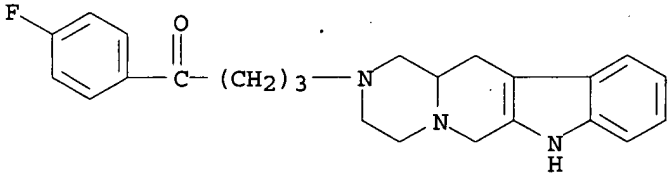
RN 55344-36-0 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



RN 55344-50-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



IT **42021-34-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., redn., and central depressant activity of)
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:156373 CAPLUS
DOCUMENT NUMBER: 82:156373
TITLE: 2-Substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-d]indole
INVENTOR(S): Saxena, Anil K.; Jain, Padam C.; Singh, Gurbakhsh; Dua, Fritzvi R.; Srimal, Rikhab C.; Dhawan, Bhola N.; Anand, Nitya
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research (India)
SOURCE: Ger. Offen., 21 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2333922	A1	19750130	DE 1973-2333922	19730704

PRIORITY APPLN. INFO.: DE 1973-2333922 19730704

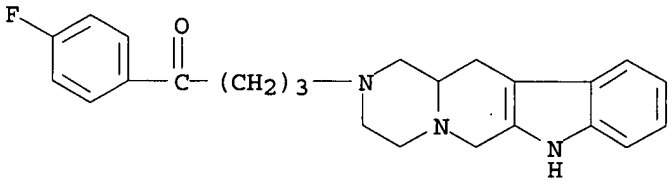
GI For diagram(s), see printed CA Issue.

AB Approx. 30 central nervous system depressants (I, R1 = e.g., H, Me, CH2CH2Ph, 4-pyridylethyl, CH2COC6H4F-p; R2 = H, Me; Y, Z = O, H2) were prepd. via cycloaddn. of II with ethylenimine (III) or ClCh2COCl and amines followed by redn. with LiAlH4. Thus, II was refluxed with III in EtOH for 24 hr to give I (R1 = R2 = H, Y = O, Z = H2) which was reduced with LiAlH4 in refluxing THF for 48 hr and treated with p-FC6H4CO(CH2)3Cl to yield I [R1 = (CH2)3COC6H4F-p, R3 = H, Y = Z = H2] (IV). IV has i.p. LD50 = 180 mg/kg in mice and orally LD50 = 700 mg/kg in rats.

IT **42021-34-1P 55344-34-8P 55344-36-0P 55344-50-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(depressant, prepn. of)

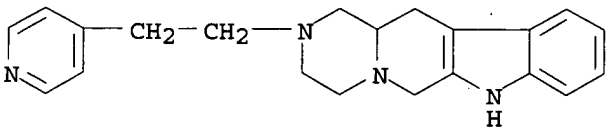
RN 42021-34-1 CAPLUS

CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



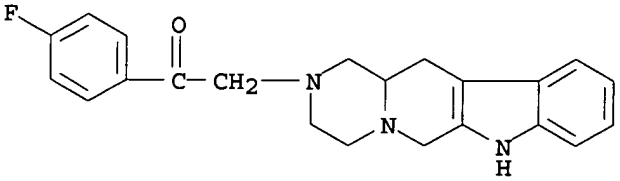
RN 55344-34-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



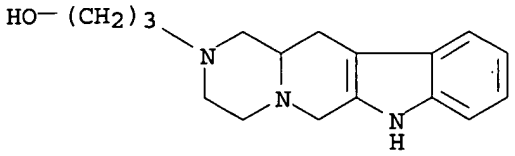
RN 55344-36-0 CAPLUS

CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)

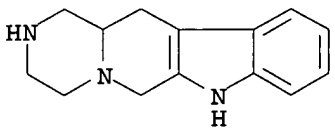


RN 55344-50-8 CAPLUS

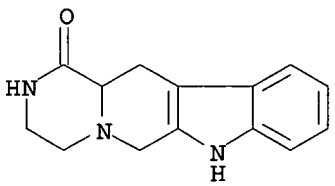
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



IT **55344-28-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reactions of)
RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro- (9CI) (CA INDEX NAME)



IT **55344-27-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)
RN 55344-27-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)

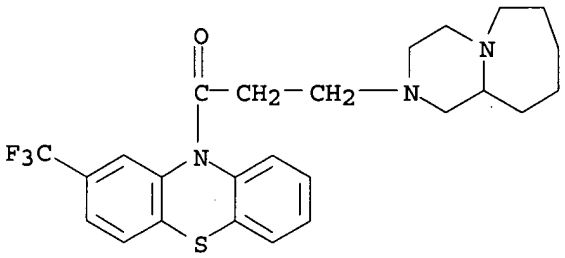


L4 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1974:83008 CAPLUS
DOCUMENT NUMBER: 80:83008
TITLE: 10-[.omega.-N-(1,4-Diazabicycloalkanyl)acyl]phenothiazines
INVENTOR(S): Likhosherstov, A. M.; Nazarova, L. S.; Skoldinov, A. P.; Markova, G. A.; Kaverina, N. V.
PATENT ASSIGNEE(S): Institute of Pharmacology, Academy of Medical Sciences, U.S.S.R.
SOURCE: Brit., 6 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

10/ 068,114

GB 1338363 A 19731121 GB 1972-10593 19720307
PRIORITY APPLN. INFO.: GB 1972-10593 19720307
GI For diagram(s), see printed CA Issue.
AB Six title compds. (I; m = 3,5; n = 1-3; R = H, Cl, CF3) and/or their acid addn. salts and methiodides, useful as coronary-dilatants and spasmolytics, were prepd. by condensing (.omega. -chloroacyl)phenothiazines with 1,4 - diazabicycloalkanes. Thus, refluxing 7.2 g 10-(.beta.-chloropropionyl)-2-(trifluoromethyl)phenothiazine with 5.04 g 1,4-diazabicyclo[4.3.0]nonane in PhMe for 3 hr gave 7.35 g I.2HCl (m = 3, n = 2, R = CF3). The results of clinical tests with I.2HCl (m = 3, n = 2, R = Cl) were reported.
IT **49780-15-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 49780-15-6 CAPLUS
CN 10H-Phenothiazine, 10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-2-(trifluoromethyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

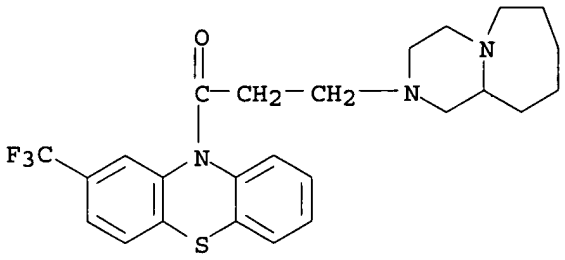
L4 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1973:526514 CAPLUS
DOCUMENT NUMBER: 79:126514
TITLE: Coronary dilating 10-[.omega.-(1,4-diazabicycloalk-4-yl)acyl]phenothiazines
INVENTOR(S): Likhosherstov, A. M.; Nazarova, L. S.; Skoldinov, A. P.; Markova, G. A.; Kaverina, N. V.
PATENT ASSIGNEE(S): Scientific-Research Institute of Pharmacology and Chemotherapy, Academy of Medical Sciences, U.S.S.R.
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2210382	A1	19730906	DE 1972-2210382	19720303
DE 2210382	C2	19820603		

PRIORITY APPLN. INFO.: DE 1972-2210382 19720303
GI For diagram(s), see printed CA Issue.
AB Twelve phenothiazines I (R = H, Cl, or CF3; n = 1-3, m = 3 or 5) or their salts were prepd. by reaction of II with 1,4-diazabicyclo[4.m.0]alkanes in an org. solvent at 50-140.degree. and were effective as coronary dilating pharmaceuticals.
IT **49780-15-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)

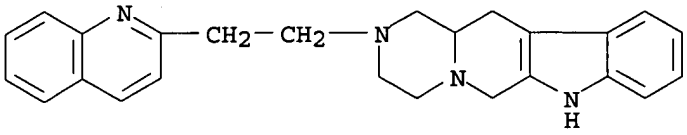
10/ 068,114

(prepn. of)
RN 49780-15-6 CAPLUS
CN 10H-Phenothiazine, 10-[3-(octahydropyrazino[1,2-a]azepin-2(1H)-yl)-1-oxopropyl]-2-(trifluoromethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

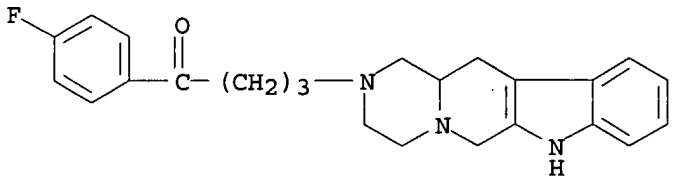


●2 HCl

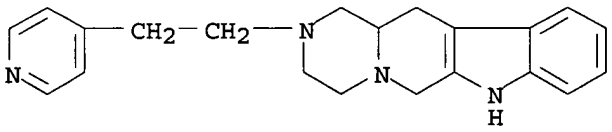
L4 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1973:461395 CAPLUS
DOCUMENT NUMBER: 79:61395
TITLE: Agents acting on the central nervous system. 15. 2-Substituted 1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indoles. New class of central nervous system depressants
AUTHOR(S): Saxena, Anil K.; Jain, Padam C.; Anand, Nitya; Dua, P. R.
CORPORATE SOURCE: Div. Med. Chem., Cent. Drug Res. Inst., Lucknow, India
SOURCE: Journal of Medicinal Chemistry (1973), 16(5), 560-4
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 2-[4-(4-Fluorophenyl)-4-oxobutyl]-1,2,3,4,6,7,12,12a-octahydropyrazino[2',1':6,1]pyrido[3,4-b]indole (I) [**41510-23-0**] and related compds. showed depressent properties in rats and mice. I produced 60% inhibition of amphetamine-induced hyperactivity in mice at 0.6 mg/kg i.p., decreased forced motor activity in mice by 50% at 7.5 mg/kg i.p., produced 50% inhibition of conditioned avoidance responses in rats at 0.15 mg/kg i.p., and counteracted amphetamine toxicity in mice by 50% at 3.5 mg/kg i.p., and was thus more potent than chlorpramazine. 2-[4-(4-Fluorophenyl)-4-hydroxybutyl]-1,2,3,4,6,7,12,12a-octahydropyrazinol[2',1':6.1]pyrido[3,4-b]indole [41510-24-1], and 2-(3-hydroxybutyl)-1,2,3,4,6,7,12,12a-octa-hydropyrazino[2',1':6,1]pyrido[3,4-b]indole [41510-25-2] were also highly active depressants. I was prepd. by converting the known dl-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylic acid [41509-88-0] to the Me ester, reacting with ethyleneimine [151-56-4] to yield dl-1-oxo-1,2,3,4,6,7,12,12a-octahydropyrazino[2,1':6,1]pyrido[3,4-b]indole [**41509-89-1**], reducing the keto group with LiAlH4, and reacting at N-2 with the appropriate chloride.
IT **42021-23-8P 42021-34-1P 55344-34-8P 55344-36-0P 55344-50-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and central nervous system depressant activity of)
RN 42021-23-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(2-quinolinyl)ethyl]- (9CI) (CA INDEX NAME)



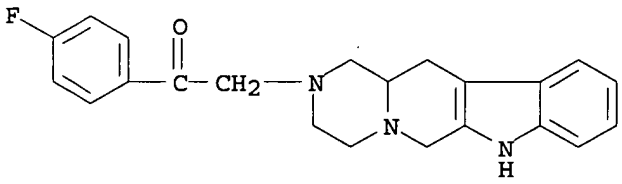
RN 42021-34-1 CAPLUS
CN 1-Butanone, 1-(4-fluorophenyl)-4-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



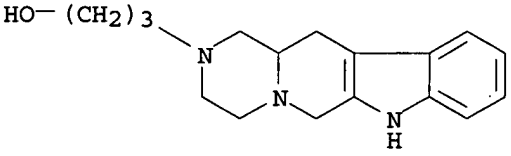
RN 55344-34-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-2-[2-(4-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 55344-36-0 CAPLUS
CN Ethanone, 1-(4-fluorophenyl)-2-(3,4,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



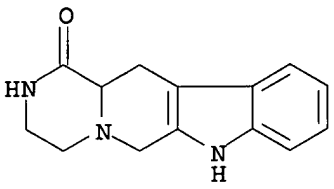
RN 55344-50-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanol, 3,4,6,7,12,12a-hexahydro- (9CI) (CA INDEX NAME)



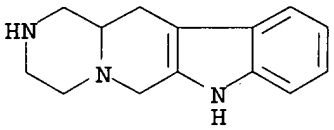
IT **55344-27-9P 55344-28-0P**

10/ 068,114

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 55344-27-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indol-1(2H)-one, 3,4,6,7,12,12a-hexahydro-
(9CI) (CA INDEX NAME)



RN 55344-28-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole, 1,2,3,4,6,7,12,12a-octahydro-
(9CI) (CA INDEX NAME)



=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	183.11	336.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-26.04	-26.04

STN INTERNATIONAL LOGOFF AT 07:41:59 ON 11 SEP 2003

10/ 068,114

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

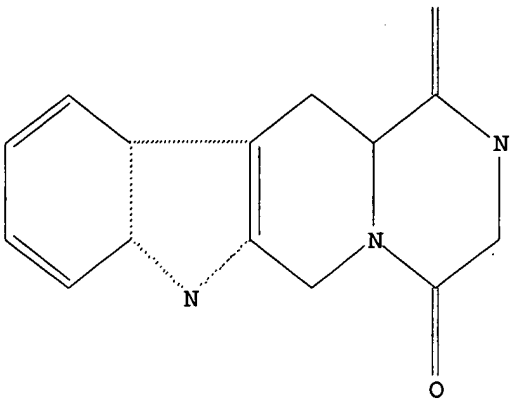
* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Feb 24	PCTGEN now available on STN
NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation
NEWS 38	AUG 18	Simultaneous left and right truncation added to ANABSTR

10/ 068,114

```
 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 07:51:19 ON 11 SEP 2003

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 07:51:28 ON 11 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     9 SEP 2003  HIGHEST RN 582289-61-0
DICTIONARY FILE UPDATES:    9 SEP 2003  HIGHEST RN 582289-61-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10068114.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
```

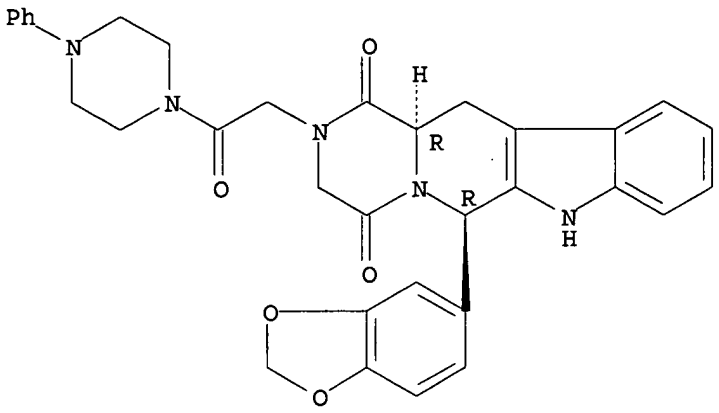
10/ 068,114



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 ful
FULL SEARCH INITIATED 07:51:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    292 TO ITERATE

100.0% PROCESSED     292 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

L2             0 SEA SSS FUL L1

=> s 'dioxo pyrazino'
        516187 'DIOXO'
         17300 'PYRAZINO'
L3          56 'DIOXO PYRAZINO'
                ('DIOXO'(W)'PYRAZINO')

=> d scan l3

L3   56 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS on STN
IN   Piperazine, 1-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-
     hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-
     4-phenyl- (9CI)
MF   C33 H31 N5 O5

Absolute stereochemistry.
```

10/ 068,114



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	157.39	157.60

FILE 'CAPLUS' ENTERED AT 07:53:17 ON 11 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 11 Sep 2003 VOL 139 ISS 11
FILE LAST UPDATED: 10 Sep 2003 (20030910/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 24 L3

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 24 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:262948 CAPLUS
DOCUMENT NUMBER: 139:159439
TITLE: Design, synthesis and biological activity of .beta.-carboline-based type-5 phosphodiesterase

10/ 068,114

inhibitors

AUTHOR(S): Maw, Graham N.; Allerton, Charlotte M. N.; Gbekor, Eugene; Million, William A.

CORPORATE SOURCE: Pfizer Global Research and Development, Department of Discovery Chemistry, Sandwich Laboratories (IPC351), Sandwich, Kent, CT13 9NJ, UK

SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(8), 1425-1428
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

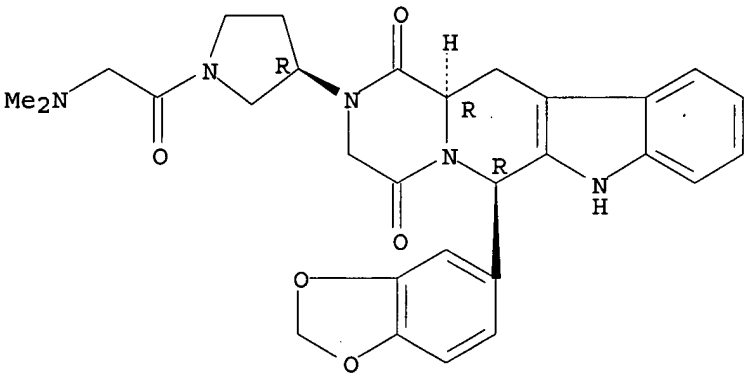
AB The SAR of a series of .beta.-carboline derived type 5 phosphodiesterase inhibitors has been explored and we have discovered compds. with excellent levels of PDE5 potency and selectivity over PDE6. However, the series exhibits low levels of selectivity over PDE11, a phosphodiesterase with unknown function.

IT **574730-13-5P 574730-14-6P 574730-15-7P 574730-16-8P 574730-17-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design, synthesis and structure-activity relationship of .beta.-carboline-based type-5 phosphodiesterase inhibitors)

RN 574730-13-5 CAPLUS

CN Pyrrolidine, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-1-[(dimethylamino)acetyl]-, (3R)- (9CI) (CA INDEX NAME)

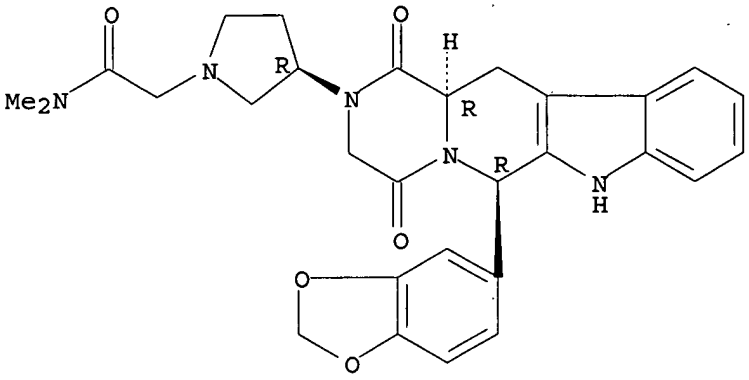
Absolute stereochemistry.



RN 574730-14-6 CAPLUS

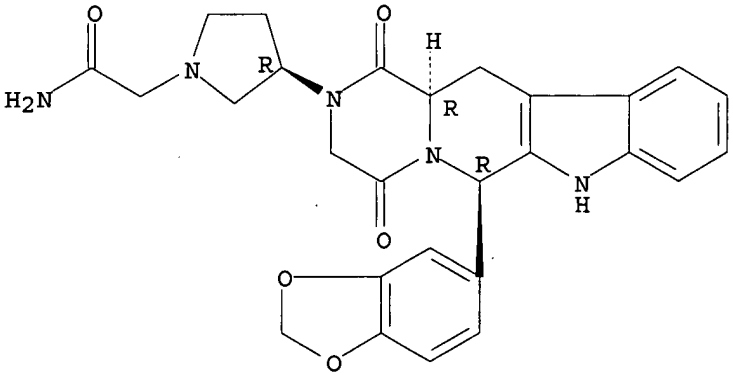
CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-N,N-dimethyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



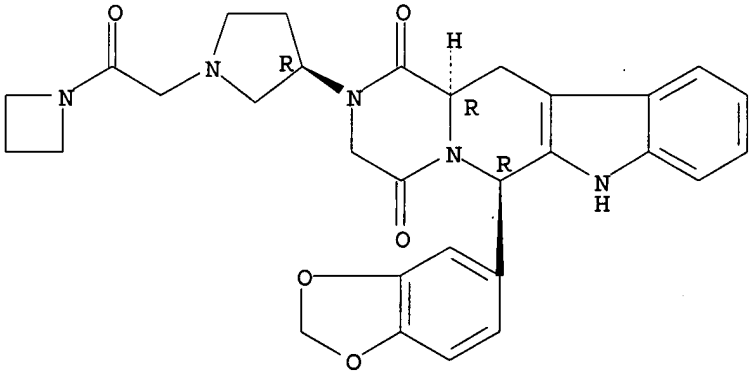
RN 574730-15-7 CAPLUS
CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 574730-16-8 CAPLUS
CN Azetidine, 1-[[(3R)-3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-1-pyrrolidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

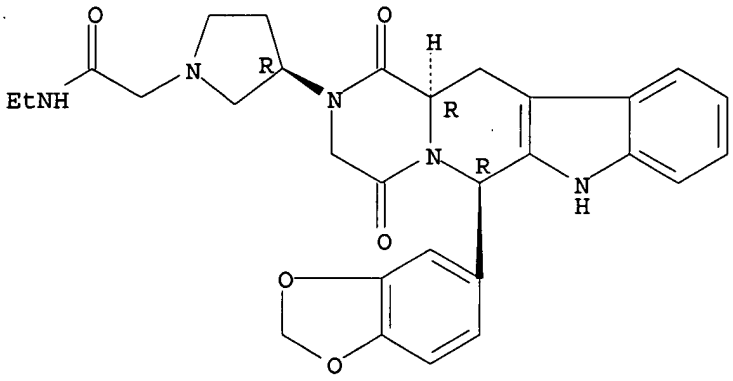


RN 574730-17-9 CAPLUS
CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-

10/ 068,114

2(1H)-yl]-N-ethyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

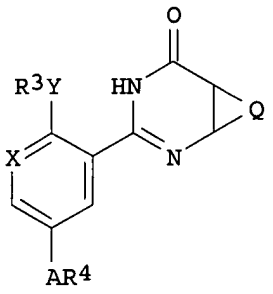


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:714162 CAPLUS
DOCUMENT NUMBER: 137:232664
TITLE: Preparation of pyrazolopyrimidines as inhibitors of guanosine 3',5'-monophosphate phosphodiesterases (cGMP PDEs).
INVENTOR(S): Barber, Christopher Gordon; Maw, Graham Nigel
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: Eur. Pat. Appl., 96 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1241170	A2	20020918	EP 2002-251367	20020227
EP 1241170	A3	20030312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002193388	A1	20021219	US 2002-93105	20020306
JP 2002322180	A2	20021108	JP 2002-68015	20020313
BR 2002000843	A	20030325	BR 2002-843	20020318

PRIORITY APPLN. INFO.: GB 2001-6631 A 20010316
US 2001-290734P P 20010514
OTHER SOURCE(S): MARPAT 137:232664
GI



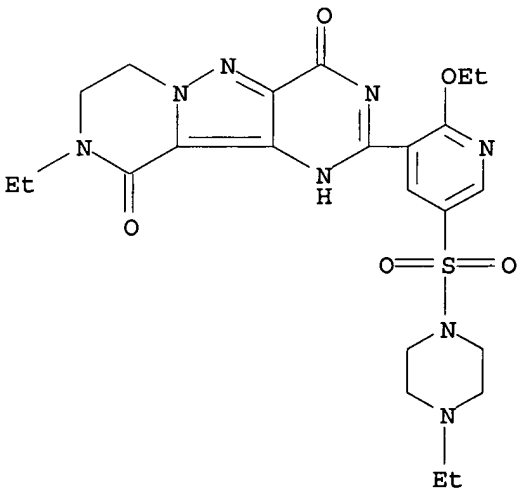
I

AB Title compds. [I; Q = (substituted) fused pyrazolo; A = SO2, CO, CH(OH); V = O, NR5; X = CH, N; R3-R5 = H, alkyl, cycloalkyl, (substituted) heterocyclyl, aryl, etc.], were prepd. e.g. for treatment of mammalian sexual disorders (no data). Thus, potassium bis(trimethylsilyl)amide was added to a soln. of 3-[[[2-ethoxy-5-[(4-ethyl-1-piperazinyl)sulfonyl]-3-pyridinyl]carbonyl]amino]-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazole-2-carboxamide (prepn. given) in ethanol and the reaction mixt. heated in a sealed vessel at 130.degree. for 16 h to give 2-[2-ethoxy-5-[(4-ethyl-1-piperazinyl)sulfonyl]-3-pyridinyl]-3,7,8,9-tetrahydro-4H-pyrrolo(2',1':5,1)pyrazolo[4,3-d]pyrimidin-4-one.

IT **459156-77-5P 459156-99-1P 459157-01-8P 459157-03-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazolopyrimidines as inhibitors of guanosine 3',5'-monophosphate phosphodiesterases)

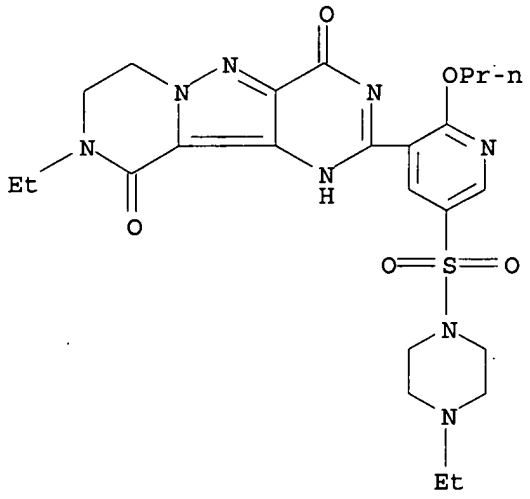
RN 459156-77-5 CAPLUS

CN Piperazine, 1-[[6-ethoxy-5-(9-ethyl-1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-3-pyridinyl]sulfonyl]-4-ethyl- (9CI) (CA INDEX NAME)

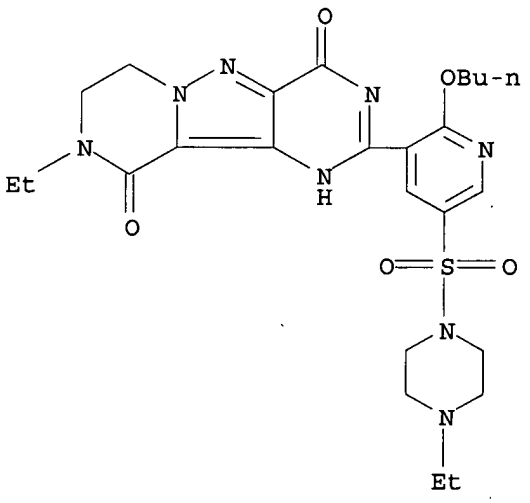


RN 459156-99-1 CAPLUS

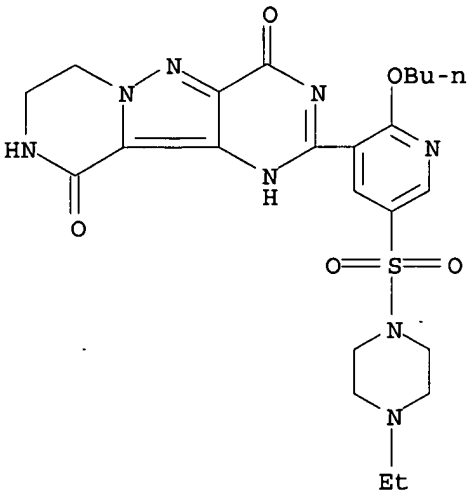
CN Piperazine, 1-ethyl-4-[[5-(9-ethyl-1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-6-propoxy-3-pyridinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 459157-01-8 CAPLUS
CN Piperazine, 1-[[6-butoxy-5-(9-ethyl-1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-3-pyridinyl]sulfonyl]-4-ethyl- (9CI) (CA INDEX NAME)



RN 459157-03-0 CAPLUS
CN Piperazine, 1-[[6-butoxy-5-(1,4,7,8,9,10-hexahydro-4,10-dioxopyrazino[1',2':1,5]pyrazolo[4,3-d]pyrimidin-2-yl)-3-pyridinyl]sulfonyl]-4-ethyl- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:328916 CAPLUS
DOCUMENT NUMBER: 137:241804
TITLE: Potent and specific inhibition of the breast cancer resistance protein multidrug transporter in vitro and in mouse intestine by a novel analogue of fumitremorgin C
AUTHOR(S): Allen, John D.; Van Loevezijn, Arnold; Lakhai, Jeany M.; Van der Valk, Martin; Van Tellingen, Olaf; Reid, Glen; Schellens, Jan H. M.; Koomen, Gerrit-Jan; Schinkel, Alfred H.
CORPORATE SOURCE: Division of Experimental Therapy, The Netherlands Cancer Institute, Amsterdam, 1066 CX, Neth.
SOURCE: Molecular Cancer Therapeutics (2002), 1(6), 417-425
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

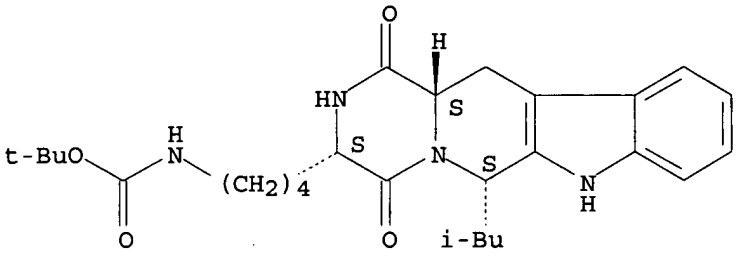
AB Inhibitors of the breast cancer resistance protein (BCRP/ABCG2) multidrug transporter are of interest as chemosensitizers for clin. drug resistance, for improving the pharmacokinetics of substrate chemotherapeutic drugs, and in functional assays of BCRP activity for tailoring chemotherapy. The fungal toxin fumitremorgin C (FTC) is a potent and specific inhibitor of BCRP, but its neurotoxic effects preclude use in vivo. We have therefore evaluated a new tetracyclic analog of FTC, Ko143, as a practical inhibitor of BCRP, comparing it with two other analogs in the same class and with GF120918. All three FTC analogs are effective inhibitors of both mouse Bcrp1 and human BCRP, proving highly active for increasing the intracellular drug accumulation and reversing Bcrp1/BCRP-mediated multidrug resistance. Indeed, Ko143 appears to be the most potent BCRP inhibitor known thus far. In contrast, the compds. have only low activity against P-glycoprotein, the multidrug resistance-assocd. protein (MRP1), or other known drug transporters. They are nontoxic in vitro at useful concns. and evinced no signs of toxicity in mice at high oral or i.p. doses. Administered p.o. to inhibit intestinal Bcrp1, Ko143 markedly increased the oral availability of topotecan in mice. It is thus the first highly potent and specific BCRP inhibitor applicable in vivo. As such, Ko143 and other FTC analogs of this type represent valuable reagents for anal. of drug resistance mechanisms and may be candidates for development as clin. BCRP inhibitors.

IT **329356-42-5**

10/ 068,114

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of breast cancer resistance protein multidrug transporter in vitro and in mouse intestine by an analog of fumitremorgin C)
RN 329356-42-5 CAPLUS
CN Carbamic acid, [4-[(3S,6S,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

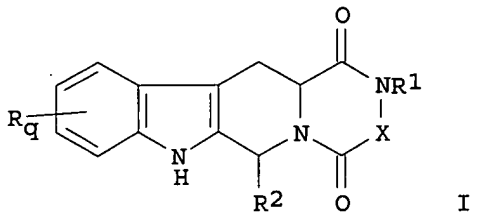


REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

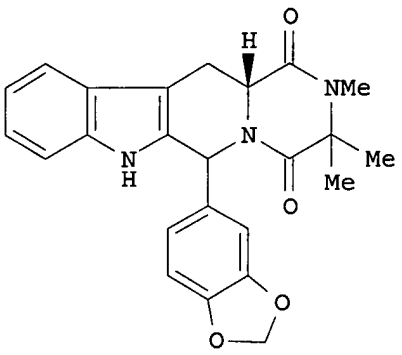
L4 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:107344 CAPLUS
DOCUMENT NUMBER: 136:151441
TITLE: Preparation of fused heterocyclic derivatives as phosphodiesterase inhibitors
INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.
PATENT ASSIGNEE(S): Lilly Icos L.L.C., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010166	A1	20020207	WO 2001-US21678	20010709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1305313	A1	20030502	EP 2001-951008	20010709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-222451P P 20000802
WO 2001-US21678 W 20010709
OTHER SOURCE(S): MARPAT 136:151441
GI



I



II

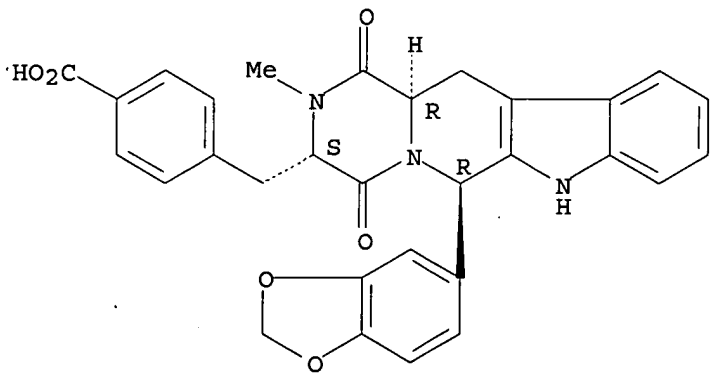
AB Compds. I [R = halo, alkyl; q = 0-4; R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, cycloalkylalkyl, arylalkyl, heteroarylalkyl; R2 is an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine or an optionally substituted bicyclic ring; X = NH or substituted imino, O, S, substituted methylene or ethylene; the substituents may form addnl. rings] and their salts and solvates were prepd. for use as phosphodiesterase (PDE) inhibitors. Thus, compd. II was prepd. by a multistep procedure starting with coupling of L-tryptophan Me ester with CbzNMeCMe2CO2H (Cbz = benzyloxycarbonyl) and showed IC50 = 161.0 nM for inhibition of cGMP-PDE.

IT **395665-59-5P 395665-72-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of fused heterocyclic derivs. as phosphodiesterase inhibitors)

RN 395665-59-5 CAPLUS

CN Benzoic acid, 4-[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]methyl]- (9CI) (CA INDEX NAME)

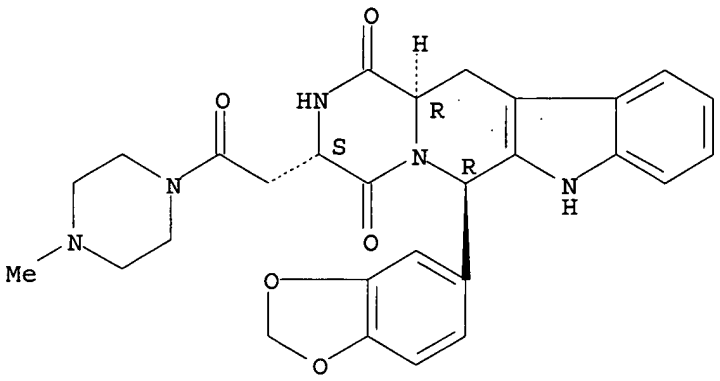
Absolute stereochemistry.



10/ 068,114

RN 395665-72-2 CAPLUS
CN Piperazine, 1-[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]acetyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

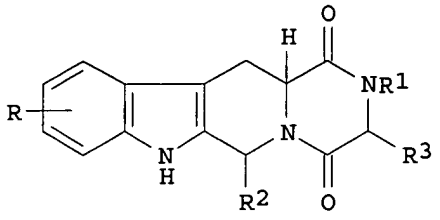


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

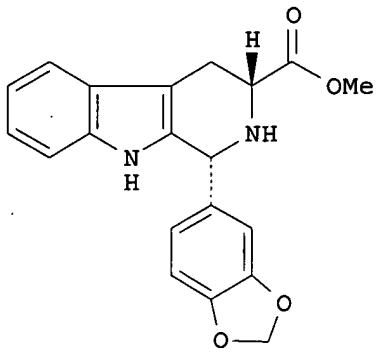
L4 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:10475 CAPLUS
DOCUMENT NUMBER: 136:85828
TITLE: Preparation of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors
INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.; Daugan, Alain Claude-Marie; Gellibert, Francoise
PATENT ASSIGNEE(S): Lilly Icos LLC, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000656	A2	20020103	WO 2001-US15935	20010515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001061707	A5	20020108	AU 2001-61707	20010515

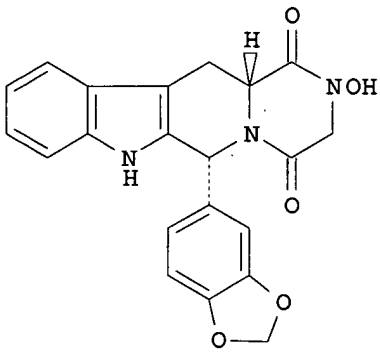
PRIORITY APPLN. INFO.: US 2000-213647P P 20000623
WO 2001-US15935 W 20010515
OTHER SOURCE(S): MARPAT 136:85828
GI



I



II



III

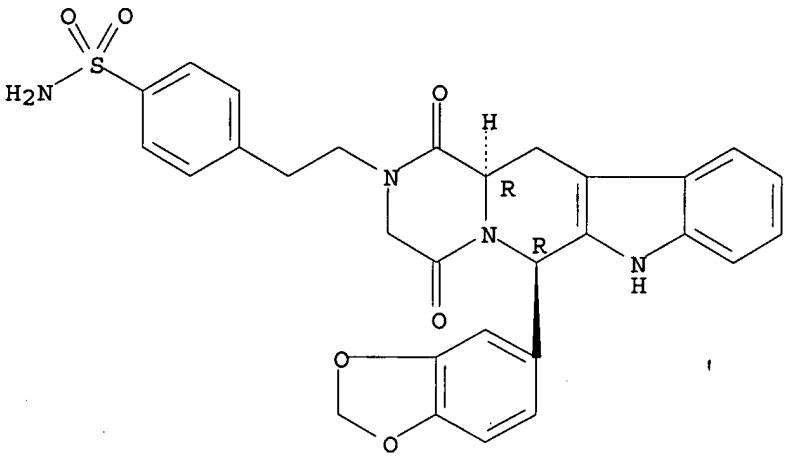
AB The pyrazinopyridoindolediones I (R = halo, C1-6-alkyl; R1 = aryl, heteroaryl, amino, R4O, R4CO, R4SO, R4SO2, C1-4-alkylene-CO2R4, C1-4-alkylenehetreroaryl, sulfamoyl, cyano, NO2, CO-C1-4-alkyleneheteroaryl, C1-4-alkylene-OR4, etc.; R2 = monocyclic arom. ring consisting of benzene, thiophene, furan, and pyridine, and an optionally substituted bicyclic ring wherein the fused ring is a 5- or 6-membered ring comprised of C and optionally heteroatoms selected from O, S, and N; R3 = H, C1-6-alkyl; R4 = H, alkyl, aryl, heteroaryl, etc.) and their salts and solvates were prepd. as cyclic GMP phosphodiesterase inhibitors. Thus, D-tryptophan Me ester hydrochloride was treated with piperonal to give the carbolinecarboxylate II, which was treated with chloroacetyl chloride followed by cyclization with hydroxylamine-HCl to give the pyrazinopyridoindoledione III. The cyclic GMP phosphodiesterase inhibitor IC50 of III 0.0075 .mu.M.

IT **385769-78-8P 385770-20-7P 385770-29-6P 385770-46-7P 385770-54-7P 385770-68-3P 385770-70-7P 385770-72-9P 385770-75-2P 385770-93-4P**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors)

RN 385769-78-8 CAPLUS

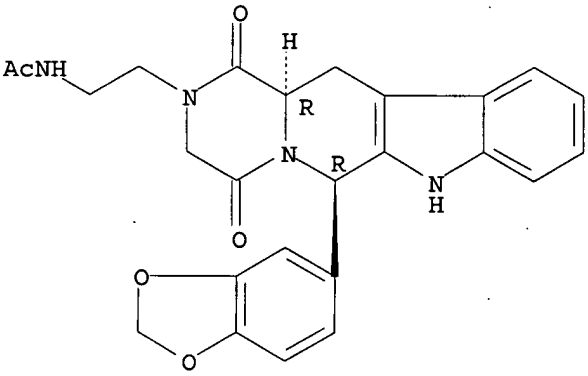
CN Benzenesulfonamide, 4-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



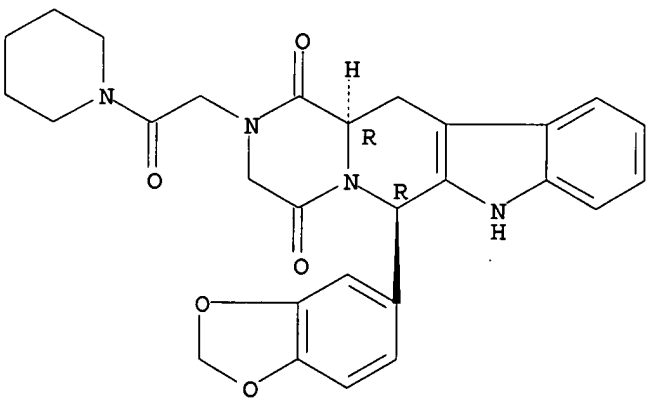
RN 385770-20-7 CAPLUS
CN Acetamide, N-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385770-29-6 CAPLUS
CN Piperidine, 1-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-(9CI) (CA INDEX NAME)

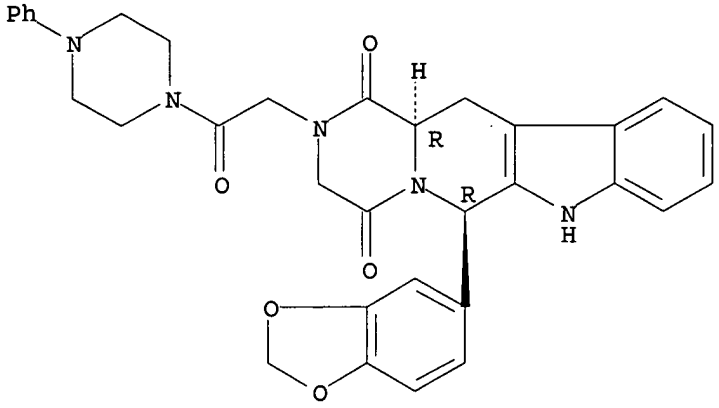
Absolute stereochemistry.



10/ 068,114

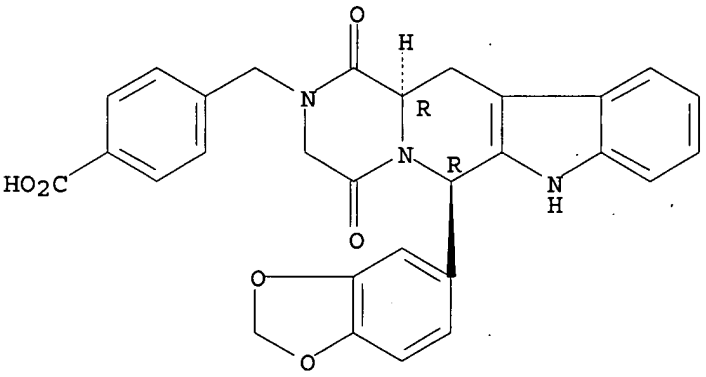
RN 385770-46-7 CAPLUS
CN Piperazine, 1-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



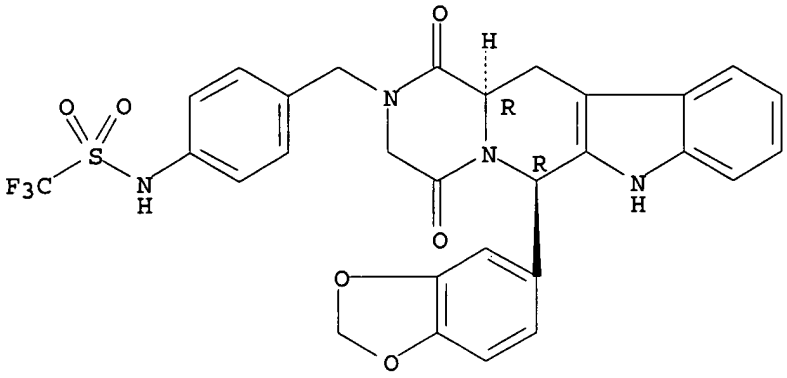
RN 385770-54-7 CAPLUS
CN Benzoic acid, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



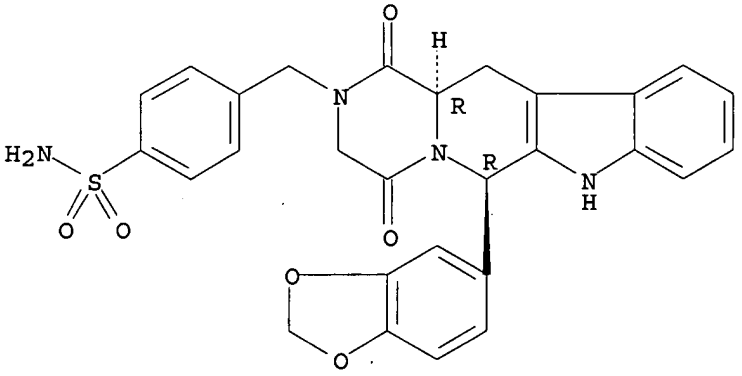
RN 385770-68-3 CAPLUS
CN Methanesulfonamide, N-[4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



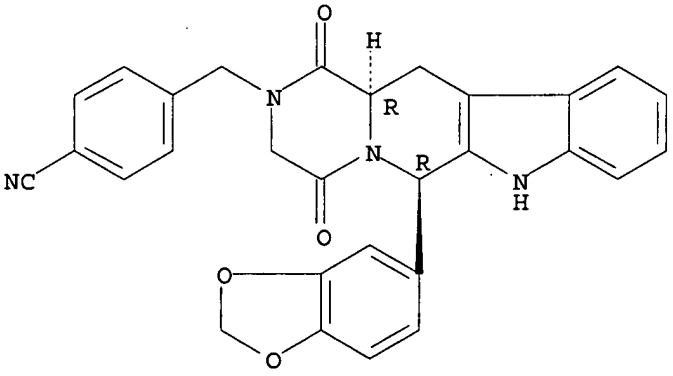
RN 385770-70-7 CAPLUS
CN Benzenesulfonamide, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385770-72-9 CAPLUS
CN Benzonitrile, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

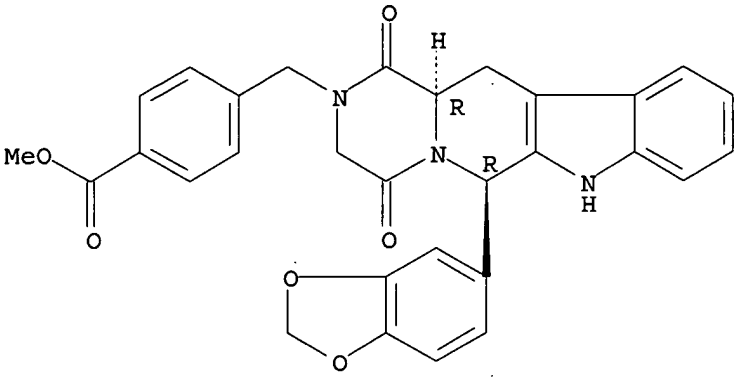


RN 385770-75-2 CAPLUS
CN Benzoic acid, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]-

10/ 068,114

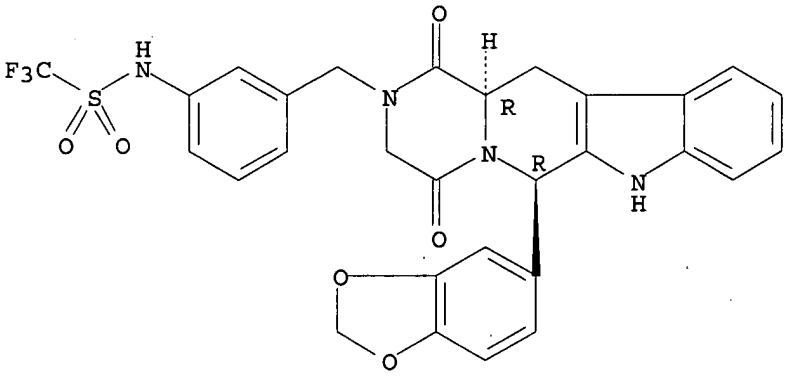
, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385770-93-4 CAPLUS
CN Methanesulfonamide, N-[3-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

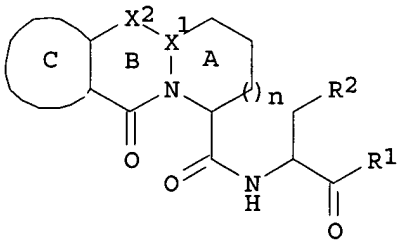


L4 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:904178 CAPLUS
DOCUMENT NUMBER: 136:37622
TITLE: Synthesis of caboxamidoquinazolines as caspase inhibitors
INVENTOR(S): Charrier, Jean-Damien; Brenchley, Guy
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

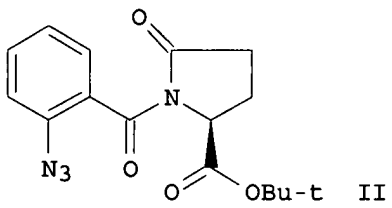
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094351	A1	20011213	WO 2001-US18243	20010605

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

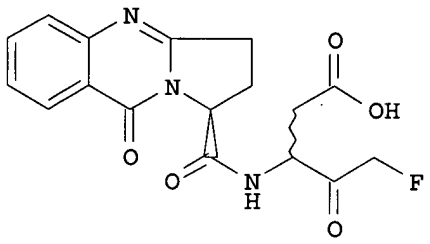
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1289993 A1 20030312 EP 2001-941972 20010605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2002045623 A1 20020418 US 2001-877832 20010607
PRIORITY APPLN. INFO.: US 2000-209929P P 20000607
WO 2001-US18243 W 20010605
OTHER SOURCE(S): MARPAT 136:37622
GI



I



II



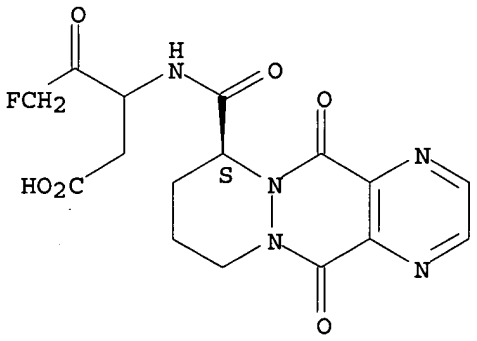
III

AB Title compds. I [R1 is H, CHN2, R, CH2Y; R is an aliph. group, an aryl group, an aralkyl group, a heterocyclic group, or a heterocyclylalkyl group; Y is an electroneg. leaving group; R2 is CO2H, CH2CO2H, or esters, amides or isosteres thereof; X2-X1 is NR3-CR3, C(R3)2-CR3, C(R3)2-N, N:C, CR3:N, C(R3):C, C(O)-N, or C(O)-C(R3); R3 is selected from hydrogen alkyl; Ring C is a fused aryl ring; n is 0 - 2; and each methylene carbon in Ring A is (un)substituted by :O or by one or more halo, alkyl or alkoxy] were prepd. Six synthetic examples were provided. E.g., (S)-5-oxoproline tert-Bu ester was acylated with 2-azidobenzoyl chloride (THF, LDA, -78.degree.C, 1 h) to give intermediate II. Azide II was treated with Ph3P (xylene, room temp.) which resulted in cyclization to the tricyclic intermediate. This intermediate was deprotected (TFA, room temp.) and the resulting carboxylic acid coupled to 3-amino-5-fluoro-4-hydroxypenatanoic acid tert-Bu ester (THF, EDC, HOBt, DMAP, room temp., 18 h) and the resulting alc. oxidized (CH2Cl2, Dess-Martin periodinane, room temp., 18 h) and finally deprotected to give (CH2Cl2, TFA, room temp., 30 min) to give III in 34% overall yield. III had Ki = 160,500 M-1s-1 for caspase-3. Example compds. also inhibited IL-1.beta. secretion and showed activity in the FAS induced apoptosis assay. I are useful for treating caspase-mediated diseases.

10/ 068,114

IT **380223-06-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of caboxamidoquinazolines as caspase inhibitors)
RN 380223-06-3 CAPLUS
CN Pentanoic acid, 5-fluoro-3-[[[(7S)-5,7,8,9,10,12-hexahydro-5,12-dioxopyrazino[2,3-d]pyridazino[1,2-a]pyridazin-7-yl]carbonyl]amino]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

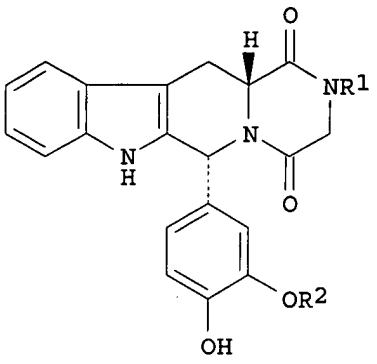
L4 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:904172 CAPLUS
DOCUMENT NUMBER: 136:20091
TITLE: Preparation of tetracyclic diketopiperazine compounds as PDE5 inhibitor
INVENTOR(S): Orme, Mark W.; Daugan, Alain Claude-Marie; Bombrun, Agnes
PATENT ASSIGNEE(S): Lilly Icos Llc, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094347	A1	20011213	WO 2001-US15937	20010515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1289990	A1	20030312	EP 2001-945961	20010515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003153575	A1	20030814	US 2002-296099	20021122

PRIORITY APPLN. INFO.: US 2000-210324P P 20000608
WO 2001-US15937 W 20010515
OTHER SOURCE(S): MARPAT 136:20091

10/ 068,114

GI



I

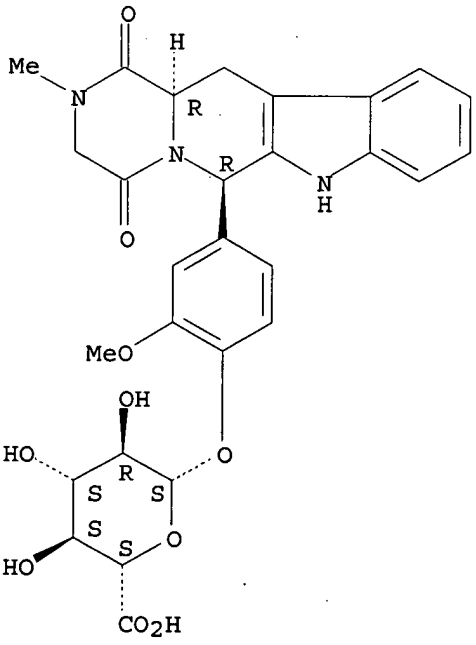
AB The title compds. I [R1 = C1-6 alkyl; R2 = H, Me] were prepd. and use of the compds. as PDE5 inhibitors was described.. E.g., (6R,12aR)-6-(3,4-dihydroxyphenyl)-2-methyl-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione was prepd. I may be used for male erectile dysfunction or female arousal disorder.

IT **378788-18-2P**
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of tetracyclic diketopiperazine compds. as PDE5 inhibitor)

RN 378788-18-2 CAPLUS

CN .beta.-D-Glucopyranosiduronic acid, 2-methoxy-4-[(6R,12aR)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

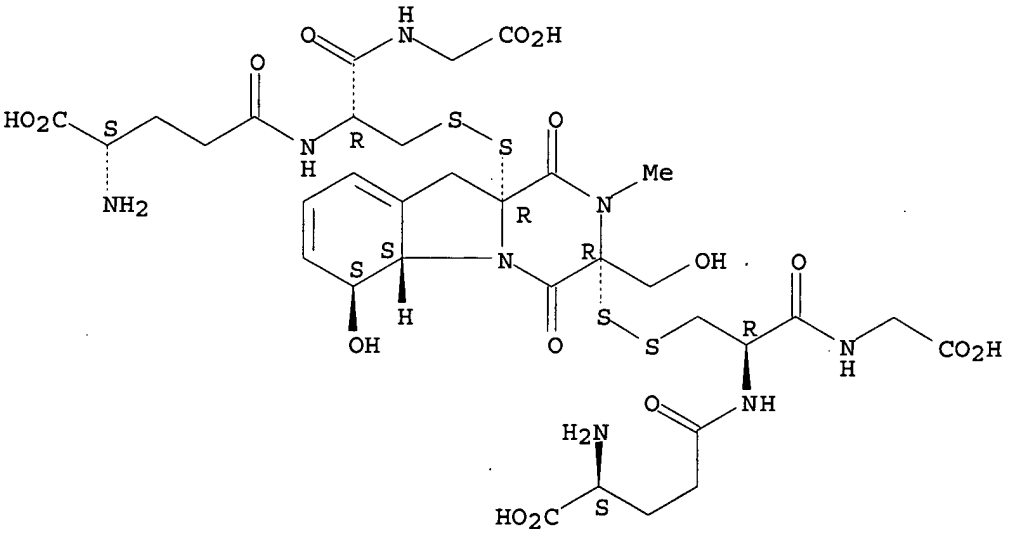
L4 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:177398 CAPLUS
DOCUMENT NUMBER: 135:29005
TITLE: Evidence for Gliotoxin-Glutathione conjugate adducts
AUTHOR(S): Bernardo, P. H.; Chai, C. L. L.; Deeble, G. J.; Liu, X.-M.; Waring, P.
CORPORATE SOURCE: Department of Chemistry, Faculties, Australian National University, 0200, Australia
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(4), 483-485
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The equil. const. for the gliotoxin/glutathione pair was found to be 1200.+-.100 M-1 at pH 7.0 at 25 .degree.C. Under conditions where the reaction was quenched rapidly with the addn. of acid, gliotoxin-glutathione conjugate adducts were detected.

IT **343946-99-6 343947-01-3 343947-03-5**
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
(evidence for gliotoxin-glutathione conjugate adducts formation)

RN 343946-99-6 CAPLUS
CN Glycine, 23,2'3-[[(3R,5aS,6S,10aR)-1,2,3,4,6,10-hexahydro-6-hydroxy-3-(hydroxymethyl)-2-methyl-1,4-dioxopyrazino[1,2-a]indole-3,10a(5aH)-diyl]bis(dithio)]bis[L-.gamma.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

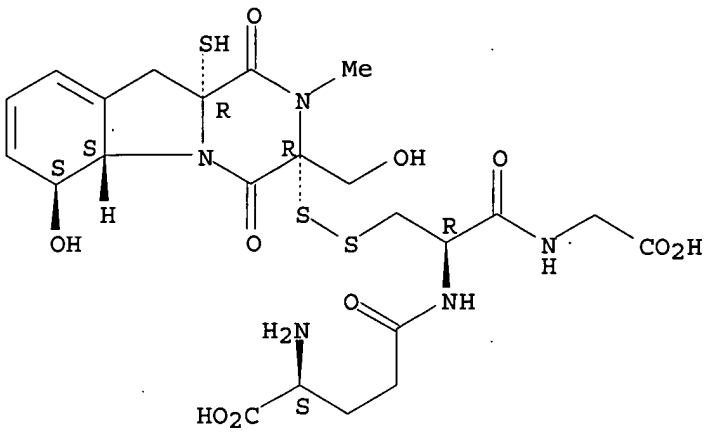
Absolute stereochemistry.



RN 343947-01-3 CAPLUS
CN Glycine, L-.gamma.-glutamyl-3-[[(3R,5aS,6S,10aR)-1,2,3,4,5a,6,10,10a-octahydro-6-hydroxy-3-(hydroxymethyl)-10a-mercapto-2-methyl-1,4-dioxopyrazino[1,2-a]indol-3-yl]dithio]-L-alanyl- (9CI) (CA INDEX NAME)

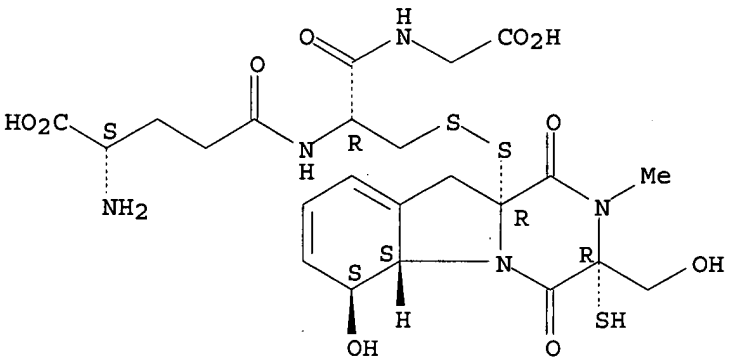
Absolute stereochemistry.

10/ 068,114



RN 343947-03-5 CAPLUS
CN Glycine, L-.gamma.-glutamyl-3-[[(3R,5aS,6S,10aR)-1,2,3,4,6,10-hexahydro-6-hydroxy-3-(hydroxymethyl)-3-mercapto-2-methyl-1,4-dioxopyrazino[1,2-a]indol-10a(5aH)-yl]dithio]-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

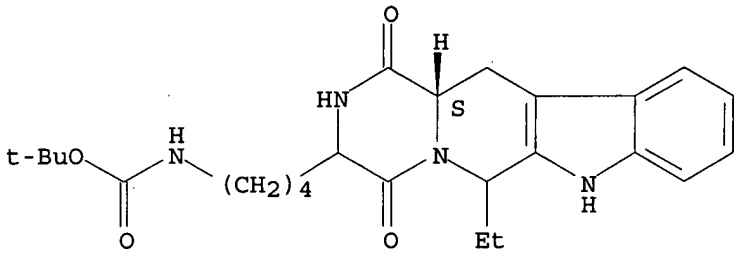
L4 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:872654 CAPLUS
DOCUMENT NUMBER: 134:216800
TITLE: Inhibition of BCRP-mediated drug efflux by fumitremorgin-type indolyl diketopiperazines
AUTHOR(S): van Loevezijn, A.; Allen, J. D.; Schinkel, A. H.; Koomen, G.-J.
CORPORATE SOURCE: Institute of Molecular Chemistry, Laboratory of Organic Chemistry, University of Amsterdam, Amsterdam, NL-1018 WS, Neth.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), Volume Date 2001, 11(1), 29-32
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A library of 42 diastereoisomeric mixts. of fumitremorgin-type indolyl diketopiperazines, prepd. by parallel solid-phase synthesis, was screened for breast cancer resistance protein inhibitory activity and compared with GF120918. Demethoxy-fumitremorgin C was synthesized (no data) by

solid-phase techniques and tested as well. Structure-activity relationship studies have identified several potent analogs, both in assays using the T6400 mouse and the T8 human cell line, whereas low cytotoxicity was seen at effective concns.

IT **211359-66-9 211359-68-1 211359-70-5 211359-71-6 329356-40-3 329356-41-4 329356-42-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of breast cancer-resistance protein-mediated drug efflux by fumitremorgin-type indolyl diketopiperazines)

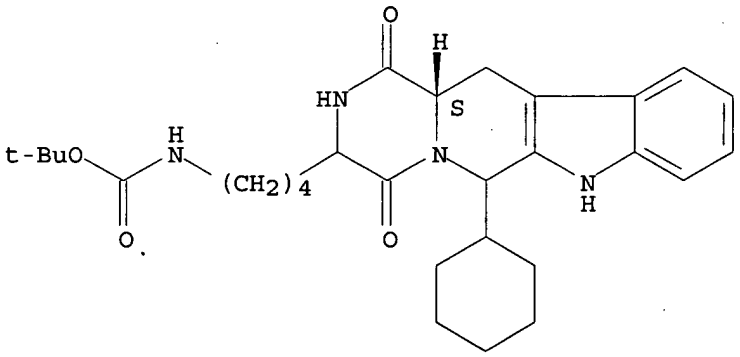
RN 211359-66-9 CAPLUS
CN Carbamic acid, [4-[(12aS)-6-ethyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 211359-68-1 CAPLUS
CN Carbamic acid, [4-[(12aS)-6-cyclohexyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

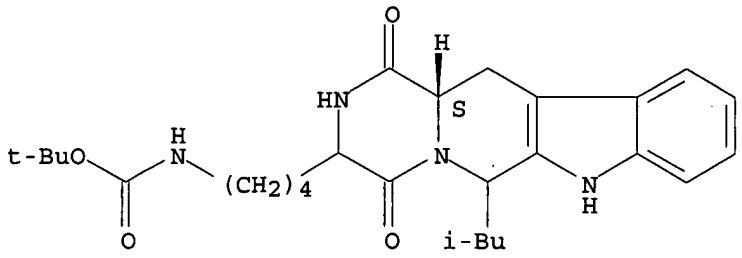
Absolute stereochemistry.



RN 211359-70-5 CAPLUS
CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

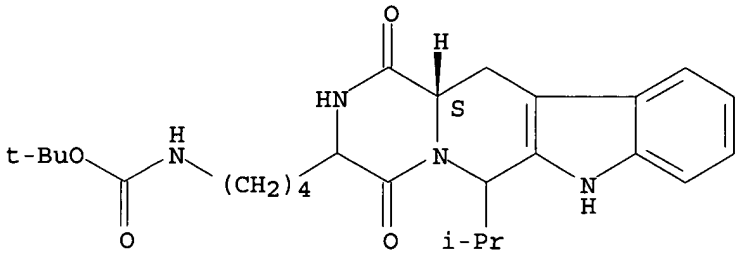
Absolute stereochemistry.

10/ 068,114



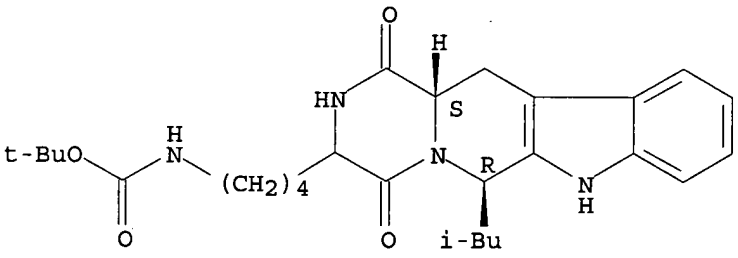
RN 211359-71-6 CAPLUS
CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(1-methylethyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



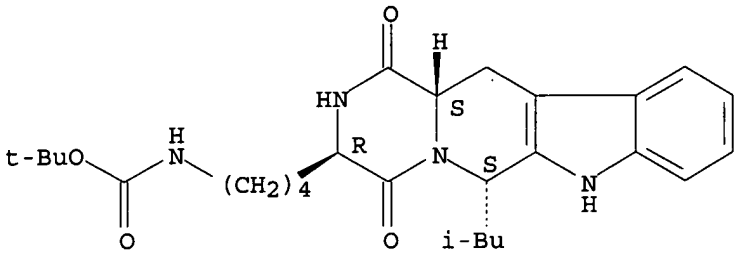
RN 329356-40-3 CAPLUS
CN Carbamic acid, [4-[(6R,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



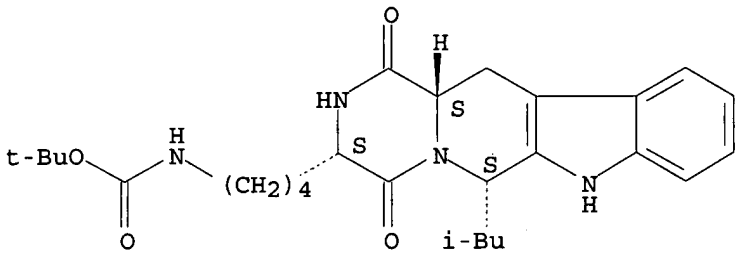
RN 329356-41-4 CAPLUS
CN Carbamic acid, [4-[(3R,6S,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 329356-42-5 CAPLUS
CN Carbamic acid, [4-[(3S,6S,12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



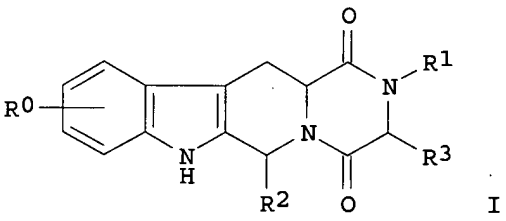
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:785898 CAPLUS
DOCUMENT NUMBER: 133:329627
TITLE: Tetracyclic cGMP-specific phosphodiesterase inhibitors and their use in disease treatment
INVENTOR(S): Daugan, Alain Claude Marie; Gellibert, Francoise
PATENT ASSIGNEE(S): Icos Corp., USA
SOURCE: U.S., 30 pp., Cont.-in-part of PCT 9519978.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6143746	A	20001107	US 1998-154051	19980916
WO 9519978	A1	19950727	WO 1995-EP183	19950119
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
WO 9703675	A1	19970206	WO 1996-EP3024	19960711
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
WO 9703985 A1 19970206 WO 1996-EP3025 19960711
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
US 6025494 A 20000215 US 1998-133078 19980812
CA 2340636 AA 20000323 CA 1999-2340636 19990826
EP 1113800 A1 20010711 EP 1999-945201 19990826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002524516 T2 20020806 JP 2000-569812 19990826
US 6127542 A 20001003 US 1999-399667 19990921
US 6369059 B1 20020409 US 2000-633431 20000807
CZ 289832 B6 20020417 CZ 2000-3428 20000919
US 2002119976 A1 20020829 US 2002-68114 20020205
PRIORITY APPLN. INFO.: GB 1994-1090 A 19940121
WO 1995-EP183 A2 19950119
GB 1995-14464 A 19950714
GB 1995-14465 A 19950714
WO 1996-EP3024 A2 19960711
WO 1996-EP3025 A2 19960711
CZ 1998-33 A3 19960711
US 1996-669389 A3 19960716
US 1998-133078 A1 19980812
US 1998-154051 A 19980916
WO 1999-US19466 W 19990826
US 1999-399667 A1 19990921
US 2000-633431 A1 20000807
OTHER SOURCE(S): MARPAT 133:329627

GI



I

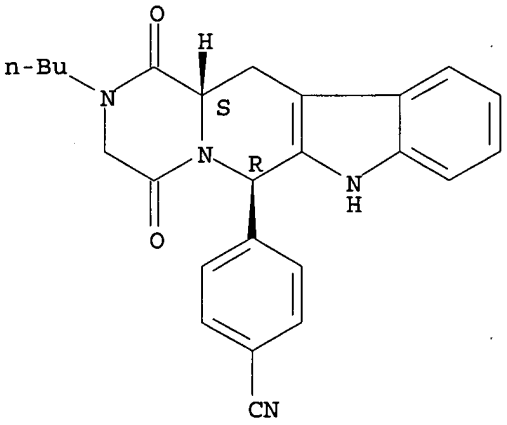
AB A compd. of formula I (R0 = H, halogen, C1-6 alkyl; R1 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, halo-C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-3 alkyl, aryl-C1-3 alkyl, heteroaryl-C1-3 alkyl; R2 = (substituted) monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine, or (substituted) bicyclic ring (a) attached to the rest of the mol. via one of the benzene ring carbon atoms, and wherein the fused ring is a 5- or 6-membered ring which may be satd. or partially or fully unsatd., and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur, and nitrogen; R3 = H, C1-3 alkyl, or R1 and R3 together = 3- or 4-membered alkyl or alkenyl chain) and salts and solvates thereof is disclosed. Compd. I is a potent and selective inhibitor of cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase, having a utility in a variety of therapeutic areas where such inhibition is beneficial, including the treatment of cardiovascular disorders and erectile dysfunction. Thus, many I compds. were synthesized and tested in vitro as inhibitors of cGMP

phosphodiesterase. Cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione showed IC50 of 10 nM.

IT **171488-69-0P 171488-89-4P 171488-90-7P 303984-33-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tetracyclic cyclic GMP-specific phosphodiesterase inhibitors and their use in disease treatment)

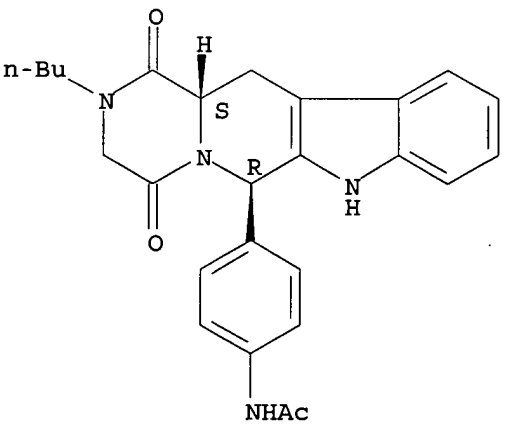
RN 171488-69-0 CAPLUS
CN Benzonitrile, 4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-89-4 CAPLUS
CN Acetamide, N-[4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

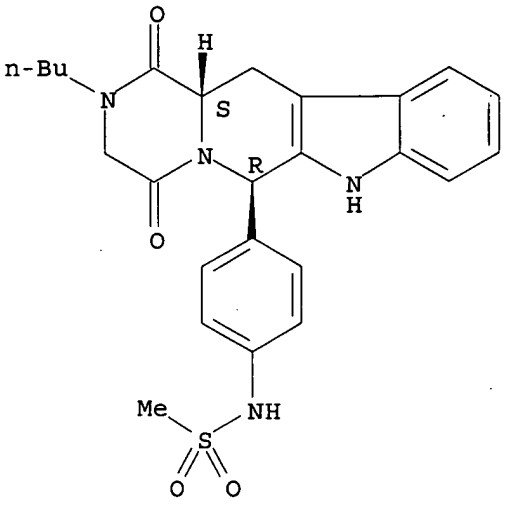
Relative stereochemistry.



RN 171488-90-7 CAPLUS
CN Methanesulfonamide, N-[4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

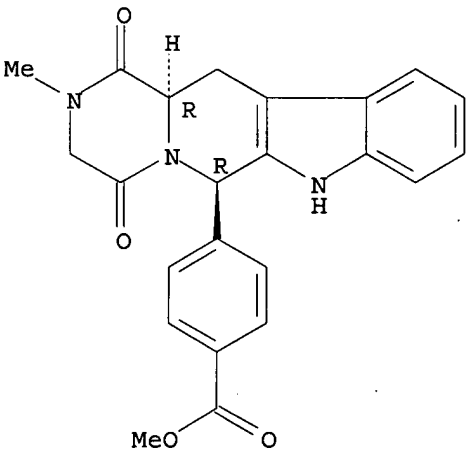
10/ 068,114

Relative stereochemistry.



RN 303984-33-0 CAPLUS
CN Benzoic acid, 4-[(6R,12aR)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:758774 CAPLUS
DOCUMENT NUMBER: 134:56943
TITLE: N-Terminal Peptide Aldehydes as Electrophiles in Combinatorial Solid Phase Synthesis of Novel Peptide Isosteres
AUTHOR(S): Groth, Thomas; Meldal, Morten
CORPORATE SOURCE: Center for Solid Phase Organic Combinatorial Chemistry, Department of Chemistry, Carlsberg Laboratory, Valby, DK-2500, Den.
SOURCE: Journal of Combinatorial Chemistry (2001), 3(1), 45-63
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society

10/ 068,114

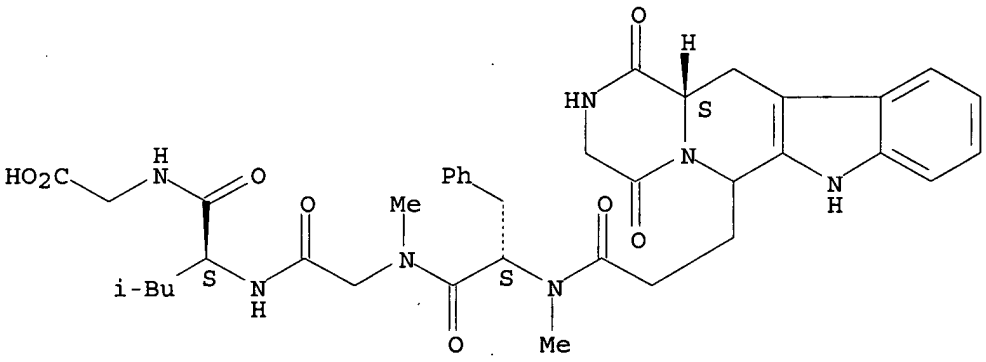
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:56943

AB N-Terminal peptide aldehydes were synthesized on a solid support and utilized as electrophiles in nucleophilic reactions in order to furnish novel and diverse peptide isosteres. The aldehyde moiety of the peptide was synthesized by coupling a protected aldehyde building block to the peptide and deprotecting it quant. in less than 3 min. It was found that protection of the two succeeding amide nitrogens was necessary in order to avoid reaction between the aldehyde and backbone amides. The N-terminal peptide aldehydes were successfully reacted in the following way: (a) reductive amination with a large variety of amines, leading to N-alkyl-.gamma.-aminobutyric peptide isosteres positioned centrally in the peptide; (b) reductive amination with amino esters, leading to N-terminal 2,5-diketopiperazine peptides; (c) Horner-Wadsworth-Emmons olefination, leading to unsatd. peptide isosteres positioned centrally in the peptide; and (d) Pictet-Spengler condensations, leading to tetrahydro-.beta.-carbolines either positioned centrally in a peptide or fused with a diketopiperazine ring in the N-terminus of the peptide.

IT **313695-12-4DP**, resin-bound **313695-13-5DP**, resin-bound **313695-14-6DP**, resin-bound
RL: SPN (Synthetic preparation); PREP (Preparation)
(terminal peptide aldehydes as electrophiles in combinatorial solid phase synthesis of novel peptide isosteres)

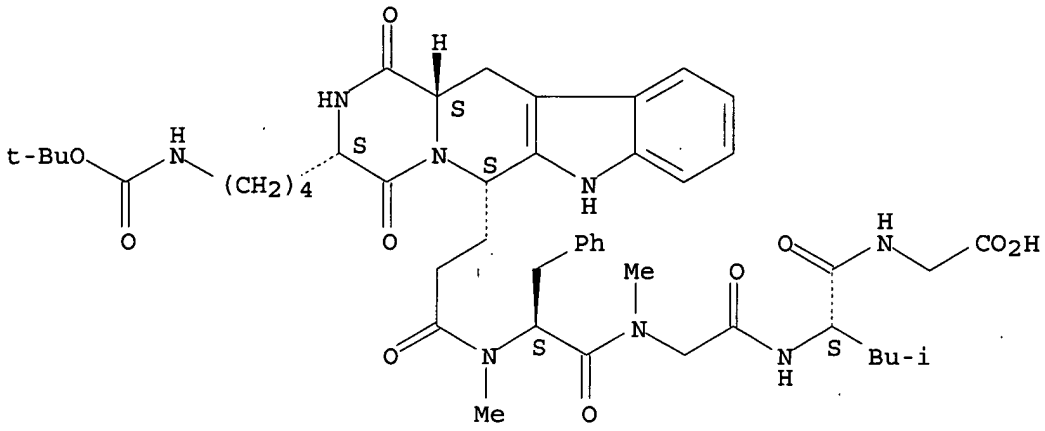
RN 313695-12-4 CAPLUS
CN Glycine, N-methyl-N-[3-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-1-oxopropyl]-L-phenylalanyl-N-methylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



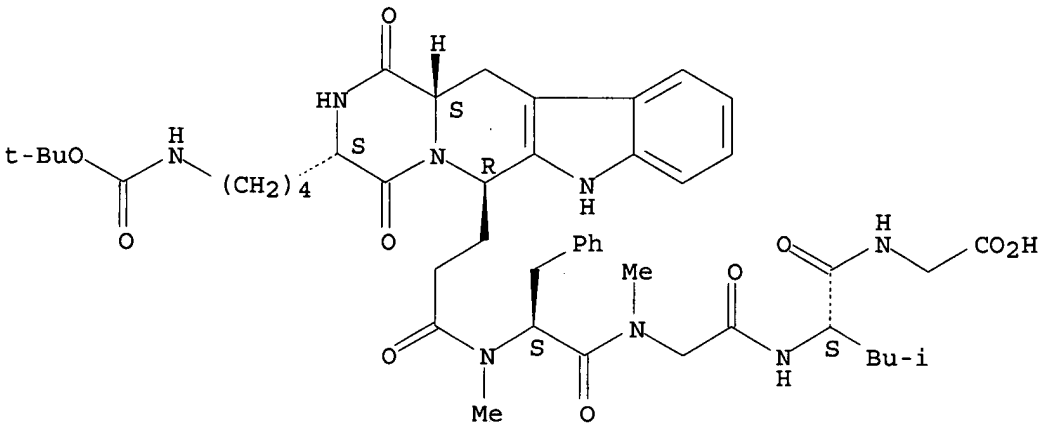
RN 313695-13-5 CAPLUS
CN Glycine, N-[3-[(3S,6S,12aS)-3-[4-[[(1,1-dimethylethoxy)carbonyl]amino]butyl]-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-1-oxopropyl]-N-methyl-L-phenylalanyl-N-methylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 313695-14-6 CAPLUS
CN Glycine, N-[3-[(3S,6R,12aS)-3-[4-[[(1,1-dimethylethoxy)carbonyl]amino]butyl]-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-1-oxopropyl]-N-methyl-L-phenylalanyl-N-methylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

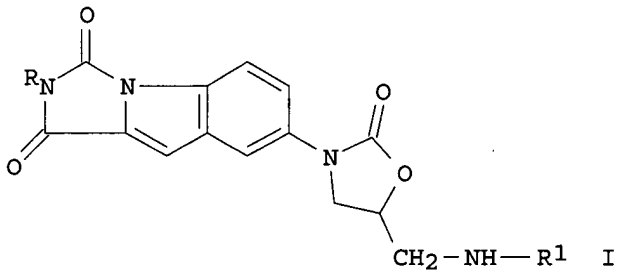


REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:487536 CAPLUS
DOCUMENT NUMBER: 131:129985
TITLE: Oxazolidines substituted by tricyclic indoles
INVENTOR(S): Ruppelt, Martin; Bartel, Stephan; Guarnieri, Walter; Raddatz, Siegfried; Rosentreter, Ulrich; Wild, Hanno; Endermann, Rainer; Kroll, Hein-Peter
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 40 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
---	---	---	---	---

DE 19802235 A1 19990729 DE 1998-19802235 19980122
WO 9937652 A1 19990729 WO 1999-EP97 19990109
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9924206 A1 19990809 AU 1999-24206 19990109
EP 1049701 A1 20001108 EP 1999-903616 19990109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002501073 T2 20020115 JP 2000-528573 19990109
PRIORITY APPLN. INFO.: DE 1998-19802235 A 19980122
WO 1999-EP97 W 19990109
OTHER SOURCE(S): MARPAT 131:129985
GI



I

AB Approx. 25 antibacterial title compds. such as I (R = benzyl, p-methoxybenzyl, allyl, Bu, cyclohexyl, Et, Me; R1 = Ac, EtCO, CO2Me) were prepd. E.g., N-[3-(2-(ethoxycarbonyl)-5-indolylamino)-2-hydroxypropyl]acetamide was cyclized with carbonyldiimidazole to give 85% 3-(2-ethoxycarbonyl-5-indolyl)-5-(acetaminomethyl)-2-oxazolidinone. The MIC of I (R = Bu, R1 = Ac) was 4 .mu.g/mL against Staphylococcus Aureus.

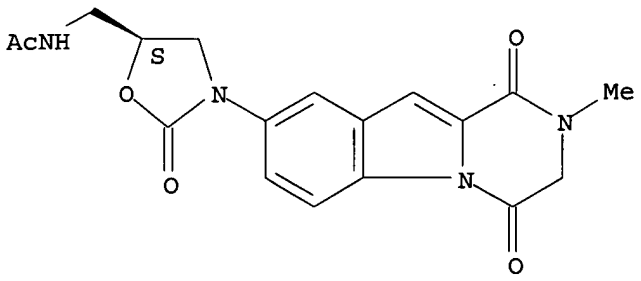
IT **234770-40-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and bactericidal activity of oxazolidines substituted by tricyclic indoles)

RN 234770-40-2 CAPLUS

CN Acetamide, N-[[(5S)-2-oxo-3-(1,2,3,4-tetrahydro-2-methyl-1,4-dioxopyrazino[1,2-a]indol-8-yl)-5-oxazolidinyl]methyl]- (9CI) (CA INDEX NAME)

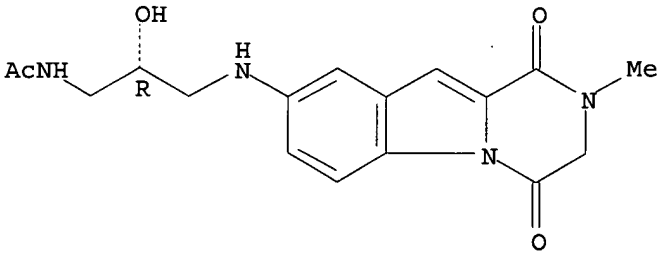
Absolute stereochemistry.

10/ 068,114



IT **234770-54-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and bactericidal activity of oxazolidines substituted by tricyclic indoles)
RN 234770-54-8 CAPLUS
CN Acetamide, N-[(2R)-2-hydroxy-3-[(1,2,3,4-tetrahydro-2-methyl-1,4-dioxopyrazino[1,2-a]indol-8-yl)amino]propyl]- (9CI) (CA INDEX NAME)

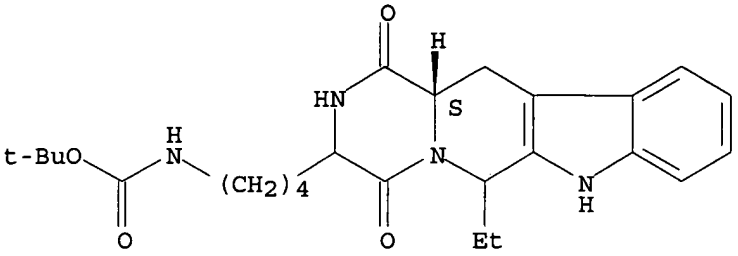
Absolute stereochemistry.



L4 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:396840 CAPLUS
DOCUMENT NUMBER: 129:175833
TITLE: Solid-phase synthesis of fumitremorgin, verruculogen and tryprostatin analogs based on a cyclization/cleavage strategy
AUTHOR(S): Van Loevezijn, Arnold; Van Maarseveen, Jan H.; Stegman, Karel; Visser, Geb M.; Koomen, Gerrit-Jan
CORPORATE SOURCE: Laboratory of Organic Chemistry, Institute of Molecular Chemistry, University of Amsterdam, Amsterdam, NL-1018 WS, Neth.
SOURCE: Tetrahedron Letters (1998), 39(26), 4737-4740
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A solid phase synthesis towards structural analogs of fumitremorgins, verruculogens and tryprostatins using a cyclization/cleavage strategy was developed. To prove the general applicability of the route, a representative set of 42 single compds. (as diastereomeric mixts.) was prepd. by parallel synthesis and analyzed with LC/MS.
IT **211359-66-9P 211359-68-1P 211359-70-5P**
211359-71-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of fumitremorgin, verruculogen and tryprostatin analogs based on a cyclization/cleavage strategy)
RN 211359-66-9 CAPLUS
CN Carbamic acid, [4-[(12aS)-6-ethyl-1,2,3,4,6,7,12,12a-octahydro-1,4-

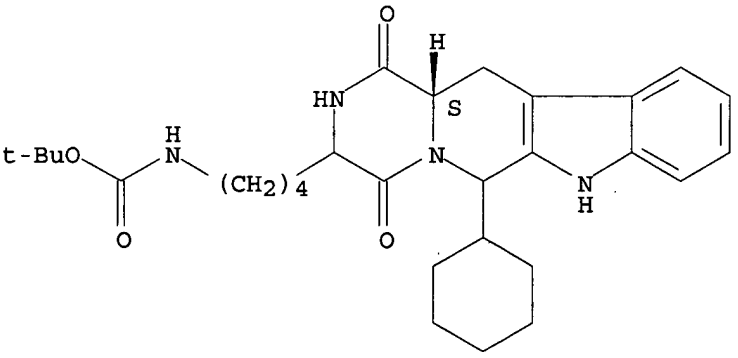
dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



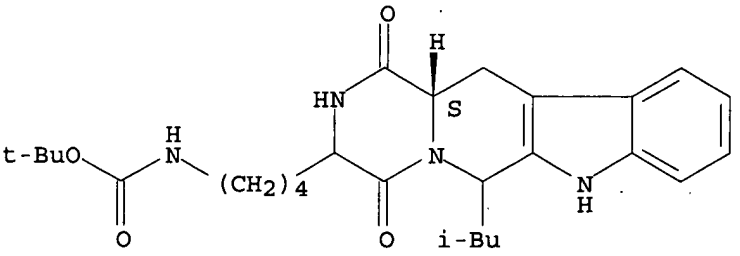
RN 211359-68-1 CAPLUS
CN Carbamic acid, [4-[(12aS)-6-cyclohexyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 211359-70-5 CAPLUS
CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(2-methylpropyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

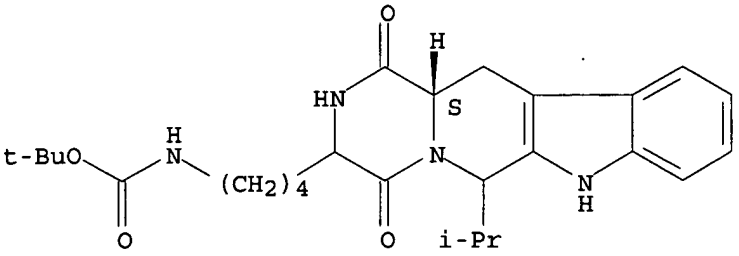
Absolute stereochemistry.



RN 211359-71-6 CAPLUS
CN Carbamic acid, [4-[(12aS)-1,2,3,4,6,7,12,12a-octahydro-6-(1-methylethyl)-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/ 068,114



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:986316 CAPLUS
DOCUMENT NUMBER: 124:55977
TITLE: Preparation of pyrazinopyridoindolediones as inhibitors of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase
INVENTOR(S): Daugan, Alain Claude-Marie
PATENT ASSIGNEE(S): Laboratoires Glaxo S.A., Fr.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9519978	A1	19950727	WO 1995-EP183	19950119
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
HR 950023	B1	20001031	HR 1995-950023	19950117
TW 378210	B	20000101	TW 1995-84100415	19950118
CA 2181377	AA	19950727	CA 1995-2181377	19950119
CA 2181377	C	20020528		
AU 9515748	A1	19950808	AU 1995-15748	19950119
AU 689205	B2	19980326		
ZA 9500424	A	19950927	ZA 1995-424	19950119
EP 740668	A1	19961106	EP 1995-907565	19950119
EP 740668	B1	19980729		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1143963	A	19970226	CN 1995-192078	19950119
CN 1045777	B	19991020		
HU 74943	A2	19970328	HU 1996-1982	19950119
JP 09508113	T2	19970819	JP 1995-519339	19950119
BR 9506559	A	19971028	BR 1995-6559	19950119
AT 169018	E	19980815	AT 1995-907565	19950119
IL 112384	A1	19980816	IL 1995-112384	19950119
ES 2122543	T3	19981216	ES 1995-907565	19950119
RU 2142463	C1	19991210	RU 1996-117127	19950119
CZ 286566	B6	20000517	CZ 1996-2116	19950119
SK 280879	B6	20000814	SK 1996-940	19950119
PL 179744	B1	20001031	PL 1995-315559	19950119
RO 117794	B1	20020730	RO 1996-1454	19950119
LV 11690	B	19970620	LV 1996-228	19960710

US 5859006	A	19990112	US 1996-669389		19960716
FI 9602927	A	19960719	FI 1996-2927		19960719
NO 9603015	A	19960909	NO 1996-3015		19960719
AU 9873912	A1	19980820	AU 1998-73912		19980626
AU 707055	B2	19990701			
US 6025494	A	20000215	US 1998-133078		19980812
US 6143746	A	20001107	US 1998-154051		19980916
CN 1224720	A	19990804	CN 1998-122779		19981201
CN 1070492	B	20010905			
HK 1013286	A1	20000519	HK 1998-114572		19981222
US 6127542	A	20001003	US 1999-399667		19990921
US 6369059	B1	20020409	US 2000-633431		20000807
US 2002119976	A1	20020829	US 2002-68114		20020205
PRIORITY APPLN. INFO.:			GB 1994-1090	A	19940121
			WO 1995-EP183	W	19950119
			GB 1995-14464	A	19950714
			GB 1995-14465	A	19950714
			WO 1996-EP3024	A2	19960711
			WO 1996-EP3025	A2	19960711
			US 1996-669389	A3	19960716
			US 1998-133078	A1	19980812
			US 1999-399667	A1	19990921
			US 2000-633431	A1	20000807

OTHER SOURCE(S): MARPAT 124:55977

GI For diagram(s), see printed CA Issue.

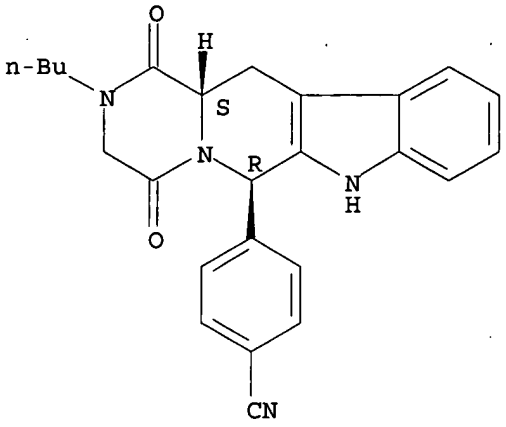
AB The title compds. I [R represents hydrogen, halogen or C1-6 alkyl; R1 represents hydrogen, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, haloC1-6alkyl, C3-8cycloalkyl, etc.; R2 represents an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan and pyridine or an optionally substituted bicyclic ring Q1 attached to the rest of the mol. via one of the benzene ring carbon atoms and wherein the fused ring A is a 5- or 6-membered ring which may be satd. or partially or fully unsatd. and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur and nitrogen; and R3 represents hydrogen or C1-3 alkyl, or R1 and R3 together represent a 3- or 4-membered alkyl or alkenyl chain] are prepd. In an in vitro test for inhibitory effect on cGMP-PDE, cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione (prepn. given) showed IC50 of 10 nM.

IT **171488-69-0P 171488-89-4P 171488-90-7P**
171489-00-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindolediones as inhibitors of cyclic guanosine monophosphate specific phosphodiesterase)

RN 171488-69-0 CAPLUS

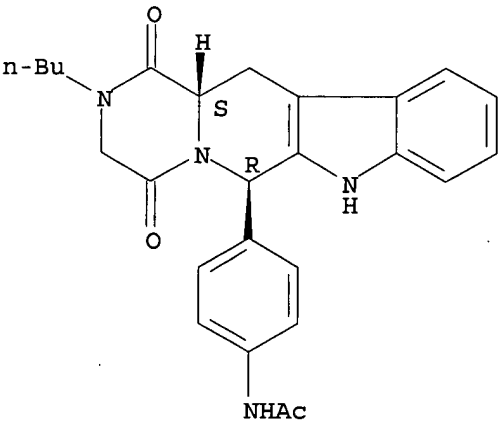
CN Benzonitrile, 4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-89-4 CAPLUS
CN Acetamide, N-[4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

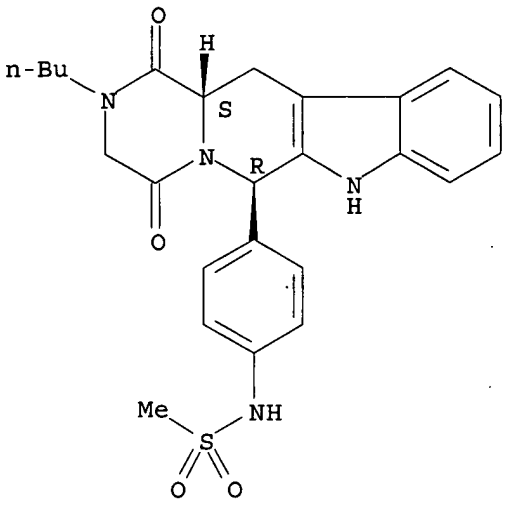
Relative stereochemistry.



RN 171488-90-7 CAPLUS
CN Methanesulfonamide, N-[4-[(6R,12aS)-2-butyl-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl]phenyl]-, rel- (9CI) (CA INDEX NAME)

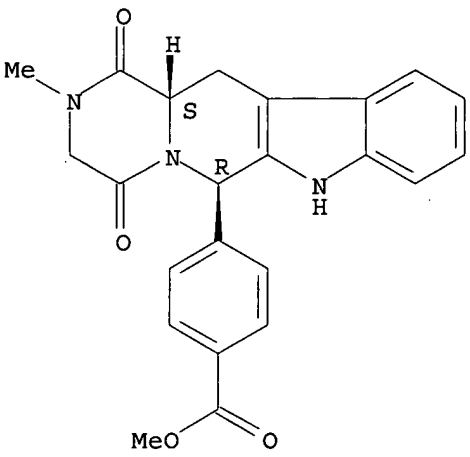
Relative stereochemistry.

10/ 068,114



RN 171489-00-2 CAPLUS
CN Benzoic acid, 4-(1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-6-yl)-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



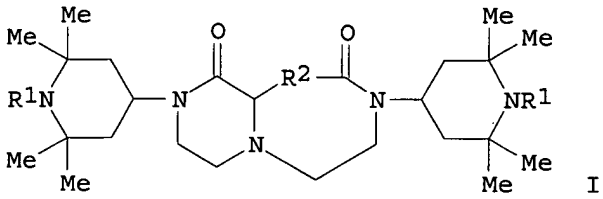
L4 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:516279 CAPLUS
DOCUMENT NUMBER: 111:116279
TITLE: Bicyclic piperidine compounds for use as stabilizers for organic materials
INVENTOR(S): Cantatore, Giuseppe; Borzatta, Valerio
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.; Ciba-Geigy S.p.A.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

10/ 068,114

EP 294329	A2	19881207	EP 1988-810337	19880525
EP 294329	A3	19890726		
EP 294329	B1	19911113		
R: DE, FR, GB, IT				
US 4859724	A	19890822	US 1988-198269	19880525
CA 1299175	A1	19920421	CA 1988-568204	19880531
JP 63316780	A2	19881226	JP 1988-136629	19880602
JP 2613088	B2	19970521		

PRIORITY APPLN. INFO.: IT 1987-20750 19870602
OTHER SOURCE(S): MARPAT 111:116279
GI

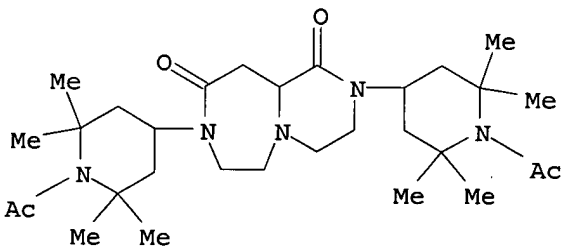


I

AB Stabilizers for org. materials, esp. synthetic polymers, are compds. having the formula I (R1 = H, O, OH, NO, CH2CN, C1-8 alkyl, allyl, benzyl, C1-8 acyl, OH-monosubstituted C2-4 alkyl, 2,3-epoxypropyl, C1-18 alkoxy, C5-12 cycloalkyloxy, 2,3-dihydroxypropyl; R2 = a direct bond or CH2). Refluxing 152.66 g N,N'-bis(2,2,6,6-tetramethyl-4-piperidyl)diethylenetriamine and 57.65 g di-Me fumarate in 150 mL trimethylbenzene for 4 h gave I (R1 = H, R2 = CH2) (II). A 50-.mu.m film made from a compn. of II 1, tris(2,4-di-tert-butylphenyl) phosphite 0.5, pentaerythritol tetrakis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate 0.5, Ca stearate 1, and polypropylene powder 1000 g had light stability 1920 h, compared with 380 h without II.

IT **121386-91-2**
RL: USES (Uses)
(stabilizers, for synthetic polymers, prepn. and use of)

RN 121386-91-2 CAPLUS
CN Piperidine, 4,4'-(octahydro-1,9-dioxopyrazino[1,2-d][1,4]diazepine-2,8-diyl)bis[1-acetyl-2,2,6,6-tetramethyl- (9CI) (CA INDEX NAME)

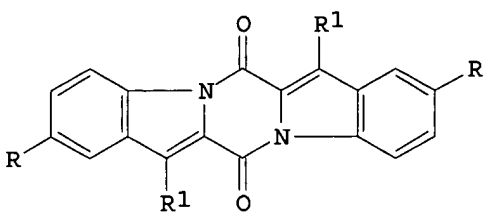


L4 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

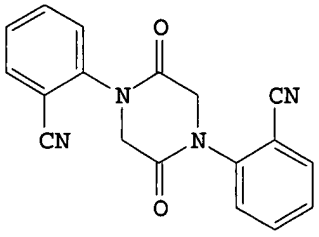
ACCESSION NUMBER:	1988:528858 CAPLUS
DOCUMENT NUMBER:	109:128858
TITLE:	One-step synthesis of pyrazino(1,2-a:4,5-a')diindole-6,13-diones
AUTHOR(S):	Schaefer, H.; Gewald, K.
CORPORATE SOURCE:	Sekt. Chem., Tech. Univ. Dresden, Dresden, Ger. Dem. Rep.
SOURCE:	Journal fuer Praktische Chemie (Leipzig) (1987),

10/ 068,114

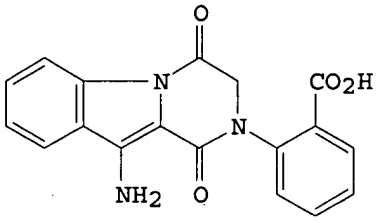
329(4), 745-8
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 109:128858
GI



I



II



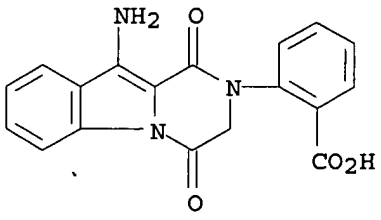
III

AB Thorpe Ziegler cyclization of 2-ClCH2CONHC6H4CN in presence of NaOMe at 120.degree. gave 56% title compd. I (R = H, R1 = NH2). Some reaction of 20.degree. gave 69% 1,4-bis(o-cyanophenyl)piperazine-2,5-dione (II). Heating II at 120.degree. in NaOMe-DMF gave 70% I (R = H, R1 = NH2). Treatment of II with 4N NaOH gave 31% pyrazinoindole-1,4-dione III. Similar reaction of o-chloroacetamino ketone in NaOMe-DMF gave I (R = H, R1 = Me; R = Cl, R1 = Ph). Dieckmann reaction of N-chloroacetylanthranilic acid Et ester with NaH-DMF gave 38% I (R = H, R1 = OH).

IT **116473-74-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 116473-74-6 CAPLUS

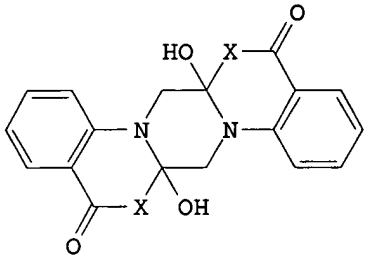
CN Benzoic acid, 2-(10-amino-3,4-dihydro-1,4-dioxopyrazino[1,2-a]indol-2(1H)-yl)- (9CI) (CA INDEX NAME)



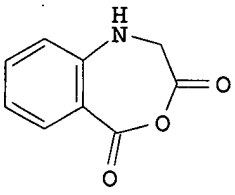
L4 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1983:143372 CAPLUS
DOCUMENT NUMBER: 98:143372
TITLE: Attempted preparation of certain benzodiazepines
AUTHOR(S): Abdel-Fattah, B.
CORPORATE SOURCE: Fac. Pharm., Univ. Cairo, Cairo, Egypt

10/ 068,114

SOURCE: Pharmazie (1982), 37(9), 637-9
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

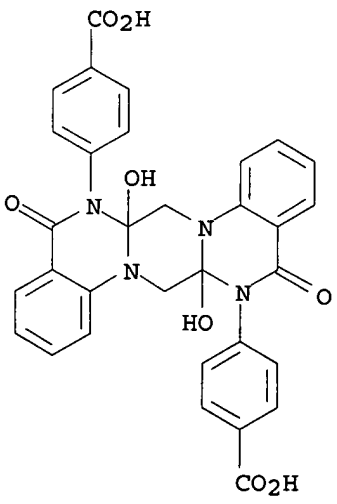


II

AB Cyclization of 2-HO2CC6H4NHCH2CO2H with Ac2O gave cyclodimer I (X = O), rather than the expected benzoxazepinedione II, a benzodiazepine intermediate. I (X = O) reacted with RNH2 [R = (un)substituted Ph, naphthyl] to give 38-68% I (X = NR).

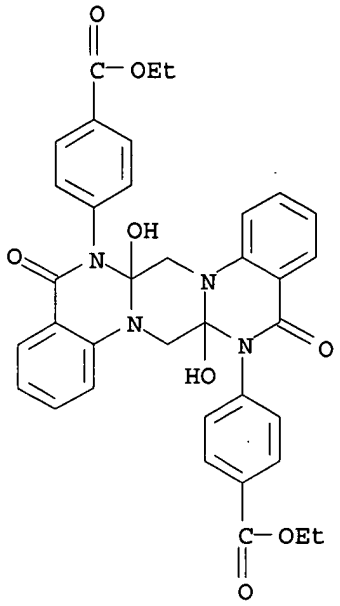
IT **84828-37-5P 84828-38-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 84828-37-5 CAPLUS
CN Benzoic acid, 4,4'-(6a,7,14a,15-tetrahydro-6a,14a-dihydroxy-5,13-dioxopyrazino[1,2-a:4,5-a']diquinazoline-6,14(5H,13H)-diyl)bis- (9CI) (CA INDEX NAME)



RN 84828-38-6 CAPLUS
CN Benzoic acid, 4,4'-(6a,7,14a,15-tetrahydro-6a,14a-dihydroxy-5,13-dioxopyrazino[1,2-a:4,5-a']diquinazoline-6,14(5H,13H)-diyl)bis-, diethyl ester (9CI) (CA INDEX NAME)

10/ 068,114



L4 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1982:200709 CAPLUS
DOCUMENT NUMBER: 96:200709
TITLE: Thermostable composition
INVENTOR(S): Chernikhov, A. Ya.; Yakovlev, M. N.; Rogov, N. S.
PATENT ASSIGNEE(S): USSR
SOURCE: Fr. Demande, 77 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2476068	A1	19810821	FR 1979-4447	19790221
FR 2476068	B1	19821203		

PRIORITY APPLN. INFO.: FR 1979-4447 19790221

AB Org. compds. which contain Si, halogen, N, S, P, B, and/or O atoms and contain NH2, OH, SH, NCO, NSO, and/or NCS groups as well as cyano and/or ethynyl groups are mixed with a filler, such as TiO2, MoS2, Al, W, Co, Cu, graphite, glass fibers, asbestos, quartz, or silica, and polymd. to prep. .apprxeq.110 heat-resistant resins which are esp. useful as binders (e.g., for abrasive particles such as diamonds and Si carbide) and adhesives. In some cases, the resins also contain a polyimide, polybenzoxazole, polyoxadiazole, polythioarylene, or similar resin which improves their mech. properties and heat resistance. Thus, 0.4 g powd. polybenzoxazole prepd. from bis(4-amino-3-hydroxyphenyl)methane and isophthalic acid was mixed with asbestos 0.8, 2,5-diamino-3,4-dicyanothiophene 0.24, and bis(4-isocyanatophenyl)methane 0.36 g and cured in a mold for 90, 90, and 30 min at 190, 250, and 300.degree., resp. The compressive strength (kg/cm2) of the molding was 1000 initially and 1150 after 500 h at 300.degree. in air.

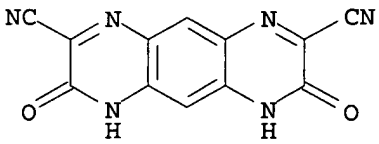
IT **80905-41-5P**
RL: PEP (Physical, engineering or chemical process); PREP (Preparation); PROC (Process)
(prepn. of heat-resistant, fillers for)
RN 80905-41-5 CAPLUS

10/ 068,114

CN Pyrazino[2,3-g]quinoxaline-2,8-dicarbonitrile, 3,4,6,7-tetrahydro-3,7-dioxo-, polymer with 3,5-diisocyanato-4-phenyl-4H-1,2,4-triazole (9CI) (CA INDEX NAME)

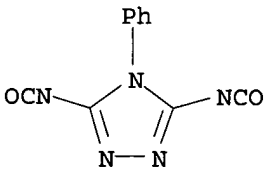
CM 1

CRN 75609-20-0
CMF C12 H4 N6 O2



CM 2

CRN 73461-00-4
CMF C10 H5 N5 O2



L4 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:640508 CAPLUS
DOCUMENT NUMBER: 93:240508
TITLE: Heat-resistant polymeric material
INVENTOR(S): Chernikhov, A. Ya.; Yakovlev, M. N.; Rogov, N. S.; Petrova, A. P.; Martirosov, E. B.; Gul, V. E.
PATENT ASSIGNEE(S): USSR
SOURCE: Ger. Offen., 83 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2907195	A1	19800828	DE 1979-2907195	19790223
JP 55118914	A2	19800912	JP 1979-24370	19790302
JP 60021647	B4	19850529		
US 4458041	A	19840703	US 1980-199116	19801017

PRIORITY APPLN. INFO.: US 1979-8562 19790201
DE 1979-2907195 19790223

AB Monomers (and, in some cases, low-mol.-wt. polymers) contg. NH2, OH, SH, NCO, NSO, and/or NCS groups as well as cyano and/or ethynyl groups are polymd. to prep. .apprx.110 polymers which are resistant to degrdn. at 300-400.degree.. In most cases, the monomers and low-mol.-wt. polymers are mixed with fillers such as TiO2, powd. metals, glass fibers, carbon fibers, graphite, powd. polyoxadiazole, polybenzoxazole, polyimide, or fluoropolymer, asbestos, MoS2, BN, silica, diamond dust, and/or SiC. The heat-resistant polymeric materials are useful as moldings, adhesives,

grinding disks, etc. Thus, a mixt. of bis(3-amino-4-cyanophenyl) ether 0.16, bis(4-isocyanatophenyl)methane 0.16, graphite 0.2, and a powd. poly-1,3,4-oxadiazole 0.78 g was molded at 130-200.degree./245 bars, demolded, and heated at 300.degree. for 30 min to prep. a molding which had compressive strength (MN/m2) 96 initially and 108 after 500 h in air at 300.degree. and had flexural strength (MN/m2) 31 initially and 35 after heat aging.

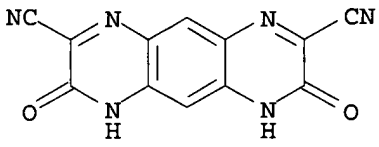
IT **75659-00-6P**
RL: PEP (Physical, engineering or chemical process); PREP (Preparation); PROC (Process)
(manuf. of heat-resistant, filler-contg.)

RN 75659-00-6 CAPLUS

CN Pyrazino[2,3-g]quinoxaline-2,8-dicarbonitrile, 3,4,6,7-tetrahydro-3,7-dioxo-, polymer with 3,5-diisocyanato-4-phenyl-4H-1,2,4-triazole and 1,2-diphenyl-1,2-dicarbadodecaborane(12) (9CI) (CA INDEX NAME)

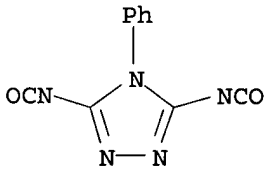
CM 1

CRN 75609-20-0
CMF C12 H4 N6 O2



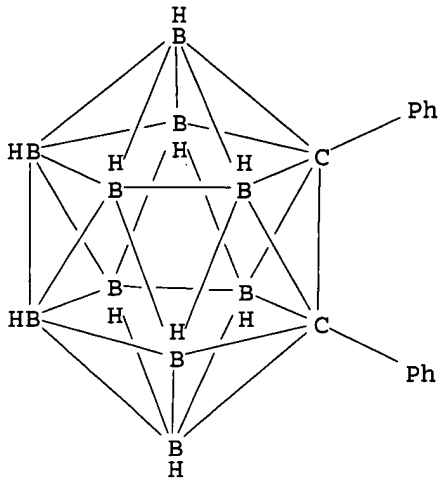
CM 2

CRN 73461-00-4
CMF C10 H5 N5 O2

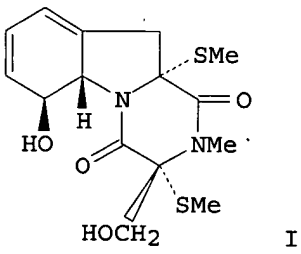


CM 3

CRN 17805-19-5
CMF C14 H20 B10



L4 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1980:446585 CAPLUS
DOCUMENT NUMBER: 93:46585
TITLE: Biosynthesis of bisdethiobis(methylthio)gliotoxin, a new metabolite of Gliocladium deliquescens
AUTHOR(S): Kirby, Gordon W.; Robins, David J.; Sefton, Mark A.; Talekar, Ratnaker R.
CORPORATE SOURCE: Dep. Chem., Univ. Glasgow, Glasgow, G12 8QQ, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1980), (1), 119-21
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

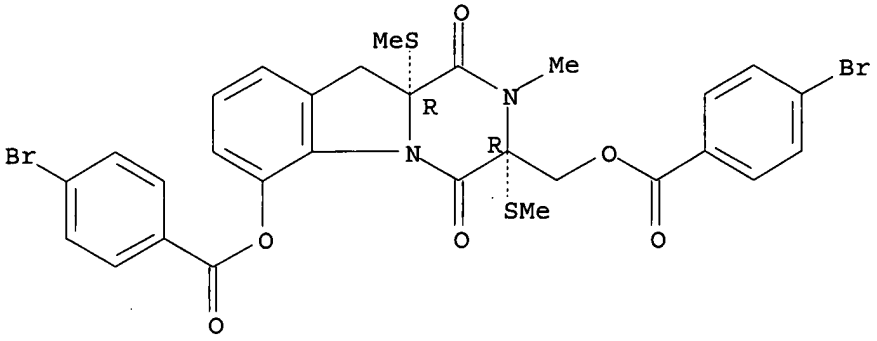


I

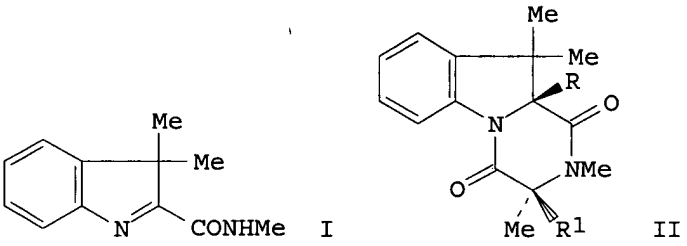
AB The title compd. (I), isolated from G. deliquescens, was identified by chem. and spectral methods. Feeding expts. showed that I is formed in G. deliquescens by irreversible redn. and methylation of gliotoxin.

IT **74181-99-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 74181-99-0 CAPLUS
CN Benzoic acid, 4-bromo-, [6-[(4-bromobenzoyl)oxy]-1,2,3,4,10,10a-hexahydro-2-methyl-3,10a-bis(methylthio)-1,4-dioxopyrazino[1,2-a]indol-3-yl]methyl ester, (3R-cis)- (9CI) (CA INDEX NAME)

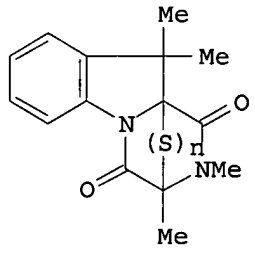
Absolute stereochemistry.



L4 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1976:560025 CAPLUS
DOCUMENT NUMBER: 85:160025
TITLE: Approaches to analogs of dehydrogliotoxin. 6. An efficient synthesis of a gliotoxin analog with anti-reverse transcriptase activity
AUTHOR(S): Ottenheijm, Henricus C. J.; Herscheid, Jacobus D. M.; Kerkhoff, Gerardus P. C.; Spande, Tom F.
CORPORATE SOURCE: Dep. Org. Chem., Cathol. Univ. Nijmegen, Nijmegen, Neth.
SOURCE: Journal of Organic Chemistry (1976), 41(21), 3433-8
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II



III

AB The addn. of MeCOCOCl to the indolenine-2-carboxamide I followed by spontaneous, diastereoselective ring closure to 3,6-disubstituted dioxopiperazines II (R = Cl, R1 = OH) provides an efficient, new synthesis of gliotoxin analogs. II (R = Cl, R1 = OH) was converted into the mercaptoalkene by treatment with H2S. Regiospecific and diastereoselective addn. of H2S to the exo methylene group gave II (R = R1 = HS). Several oxidn. procedures were studied for the conversion of II (R = R1 = HS) into disulfide III (n = 2). III (n = 2,3) were obtained from II (R = R1 = HS) by reaction with SCl2 and S2Cl2, resp.; the monosulfide

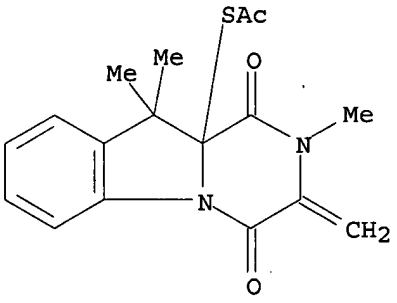
10/ 068,114

III (n = 1) was prepd. from III (n = 2) by treatment with Ph3P. Analogs between this synthesis and what is known about the biosynthesis of gliotoxin are discussed. III (n = 2) (81% overall yield) inhibits the enzyme reverse transcriptase, while having no effect on transcriptase; its activity is comparable to that of gliotoxin.

IT **59888-46-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 59888-46-9 CAPLUS

CN Ethanethioic acid, S-(1,2,3,4-tetrahydro-2,10,10-trimethyl-3-methylene-1,4-dioxopyrazino[1,2-a]indol-10a(10H)-yl) ester (9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1976:43989 CAPLUS

DOCUMENT NUMBER: 84:43989

TITLE: Three-step synthesis of a gliotoxin analog with antireverse transcriptase activity

AUTHOR(S): Ottenheijm, Henricus C. J.; Kerkhoff, Gerardus P. C.; Bijen, Johannes W. H. A.; Spande, Tom F.

CORPORATE SOURCE: Dep. Org. Chem., Univ. Nijmegen, Nijmegen, Neth.

SOURCE: Journal of the Chemical Society, Chemical Communications (1975), (19), 768-9
CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

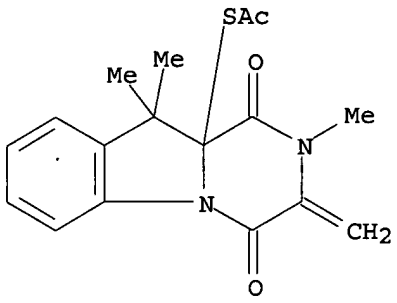
GI For diagram(s), see printed CA Issue.

AB A method of general applicability to the prepn. of analogs of gliotoxin involved addn. of Me(CO)2Cl to the carboxamide I, prepd. by condensation of Et 3,3-dimethylindolenine-2-carboxylate and MeNH2, followed by cyclization of the Leuchs' adduct formed to give II (R = Cl, R1 = OH). Treatment of II (R = Cl, R1 = OH) with H2S-ZnCl2 at 0.degree. gave the cis-dithiol II (R = R1 = SH) which underwent oxidn. to give 37% disulfide III (n = 2) and thionation to give III (n = 4). Treatment of III (n = 2) with PPh3 in EtOH gave 20% III (n = 1). III (n = 2) inhibited reverse transcriptase, the RNA-dependent DNA polymerases of RNA tumor viruses.

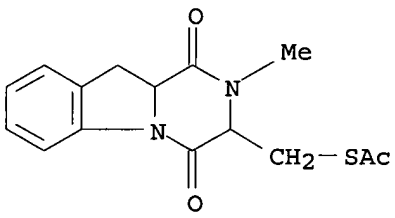
IT **59888-46-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 59888-46-9 CAPLUS

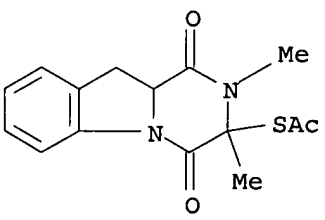
CN Ethanethioic acid, S-(1,2,3,4-tetrahydro-2,10,10-trimethyl-3-methylene-1,4-dioxopyrazino[1,2-a]indol-10a(10H)-yl) ester (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1975:578991 CAPLUS
DOCUMENT NUMBER: 83:178991
TITLE: Convenient synthesis of dioxopiperazines via aminolysis of .alpha.-(pyruvylamino) esters
AUTHOR(S): Marshall, J. A.; Schlaf, T. F.; Csernansky, J. G.
CORPORATE SOURCE: Dep. Chem., Northwest. Univ., Evanston, IL, USA
SOURCE: Synthetic Communications (1975), 5(3), 237-44
CODEN: SYNCAV; ISSN: 0039-7911
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Dioxopiperazines I and II were prepd. from indoline III by cyclizing with MeNH2 to give dioxopiperazine IV, which was dehydrated to methylene compd. V. V added AcSH to give I and II. Analogous reactions starting with pyrrole VI gave dioxopiperazine VII.
IT **57101-32-3P 57101-33-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 57101-32-3 CAPLUS
CN Ethanethioic acid, S-[(1,2,3,4,10,10a-hexahydro-2-methyl-1,4-dioxopyrazino[1,2-a]indol-3-yl)methyl] ester (9CI) (CA INDEX NAME)

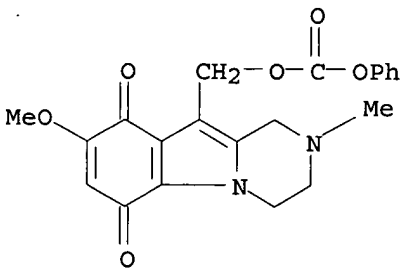


RN 57101-33-4 CAPLUS
CN Ethanethioic acid, S-(1,2,3,4,10,10a-hexahydro-2,3-dimethyl-1,4-dioxopyrazino[1,2-a]indol-3-yl) ester (9CI) (CA INDEX NAME)



10/ 068,114

L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1972:113169 CAPLUS
DOCUMENT NUMBER: 76:113169
TITLE: Synthesis of mitomycin analogs. I. Synthesis of 2-methylpiperazino[1,2-a]indole-6,9-diones
AUTHOR(S): Yamada, Yasuhiro; Takai, Haruki; Hatano, Kota; Sakakibara, Masayuki; Matsui, Masanao
CORPORATE SOURCE: Dep. Agric. Chem., Univ. Tokyo, Tokyo, Japan
SOURCE: Agricultural and Biological Chemistry (1972), 36(1), 106-11
CODEN: ABCHA6; ISSN: 0002-1369
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Alkylation of the indolecarboxylate (I) with Et bromoacetate and NaH in THF, followed by reaction with MeNH2 and heating, gave a dione (II). Redn. of II, followed by formylation, yielded the aldehyde (III). Nitration of III followed by redn. gave the aminoaldehyde (IV). Oxidn. of IV followed by redn. gave a hydroquinone, which on oxidn. gave the 2-methylpiperazino[1,2-a]-indole-6,9-dione (V, R1 = H, R2 = OMe), from which were prepd. V (R1 = CONH2, CONHMe; R2 = NH2, OMe). V (R1 = CONH2, R2 = OMe), e.g., was effective in vitro against, e.g., Staphylococcus aureus at min. inhibitory concn. 0.19 .mu.g/ml.
IT **35727-35-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 35727-35-6 CAPLUS
CN Carbonic acid, (1,2,3,4,6,9-hexahydro-8-methoxy-2-methyl-6,9-dioxopyrazino[1,2-a]indol-10-yl)methyl phenyl ester (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 07:51:19 ON 11 SEP 2003)

FILE 'REGISTRY' ENTERED AT 07:51:28 ON 11 SEP 2003
L1 STRUCTURE UPLOADED
L2 0 S L1 FUL
L3 56 S 'DIOXO PYRAZINO'

FILE 'CAPLUS' ENTERED AT 07:53:17 ON 11 SEP 2003
L4 24 S L3

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	109.70	267.30

10/ 068,114

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-15.62	-15.62

STN INTERNATIONAL LOGOFF AT 07:54:37 ON 11 SEP 2003